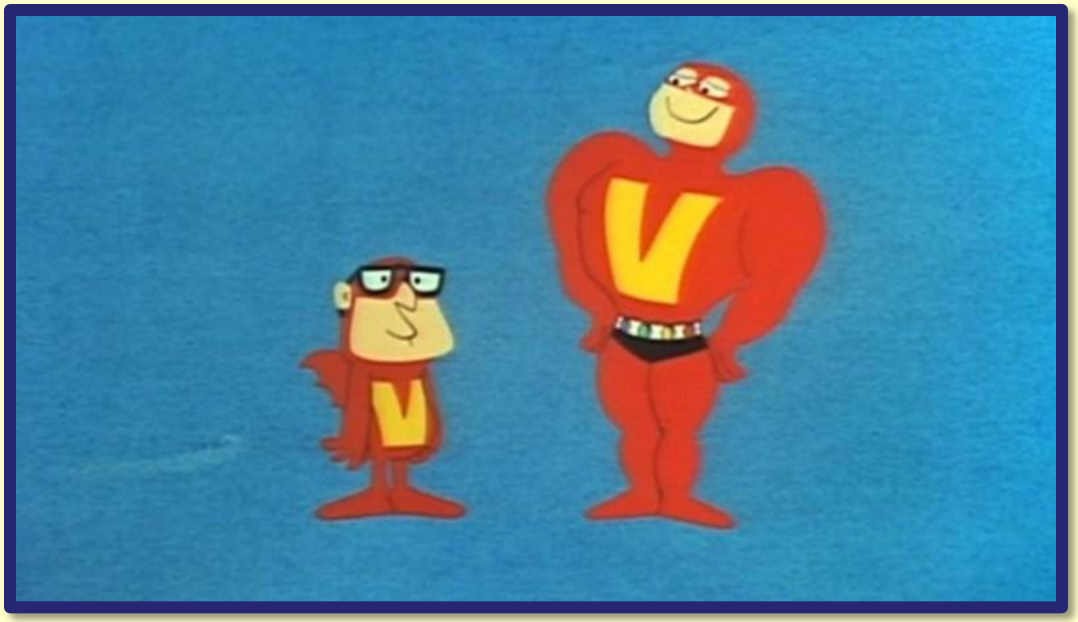
I SUPER BATTERI: l'inesorabile evoluzione dell'antibioticoresistenza

Mario Sarti
Laboratorio Provinciale
di Microbiologia Clinica
NOCSAE (Baggiovara)

Modena 28-11-12



Batteri

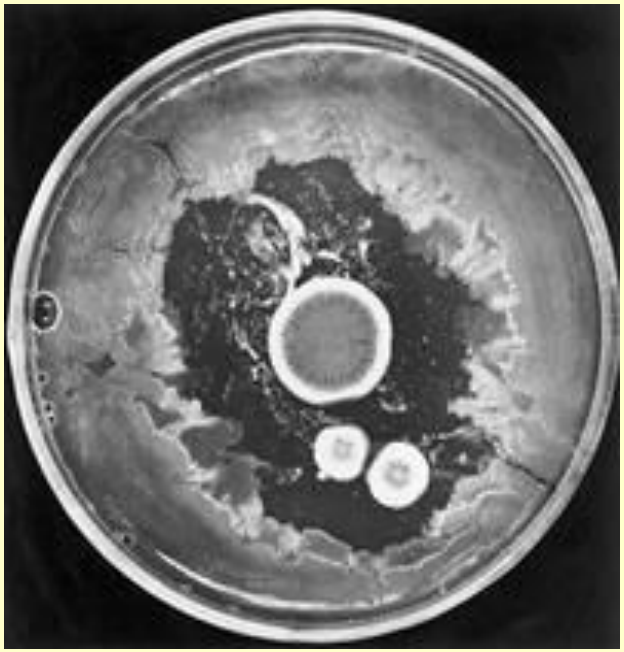
- Organismi unicellulari
- ubiquitari
- molte specie colonizzano il corpo umano
- in alcune particolari circostanze possono diventare patogene

breve storia degli antibiotici:

1869

Vincenzo Tiberio

1929



Alexander Fleming

1935

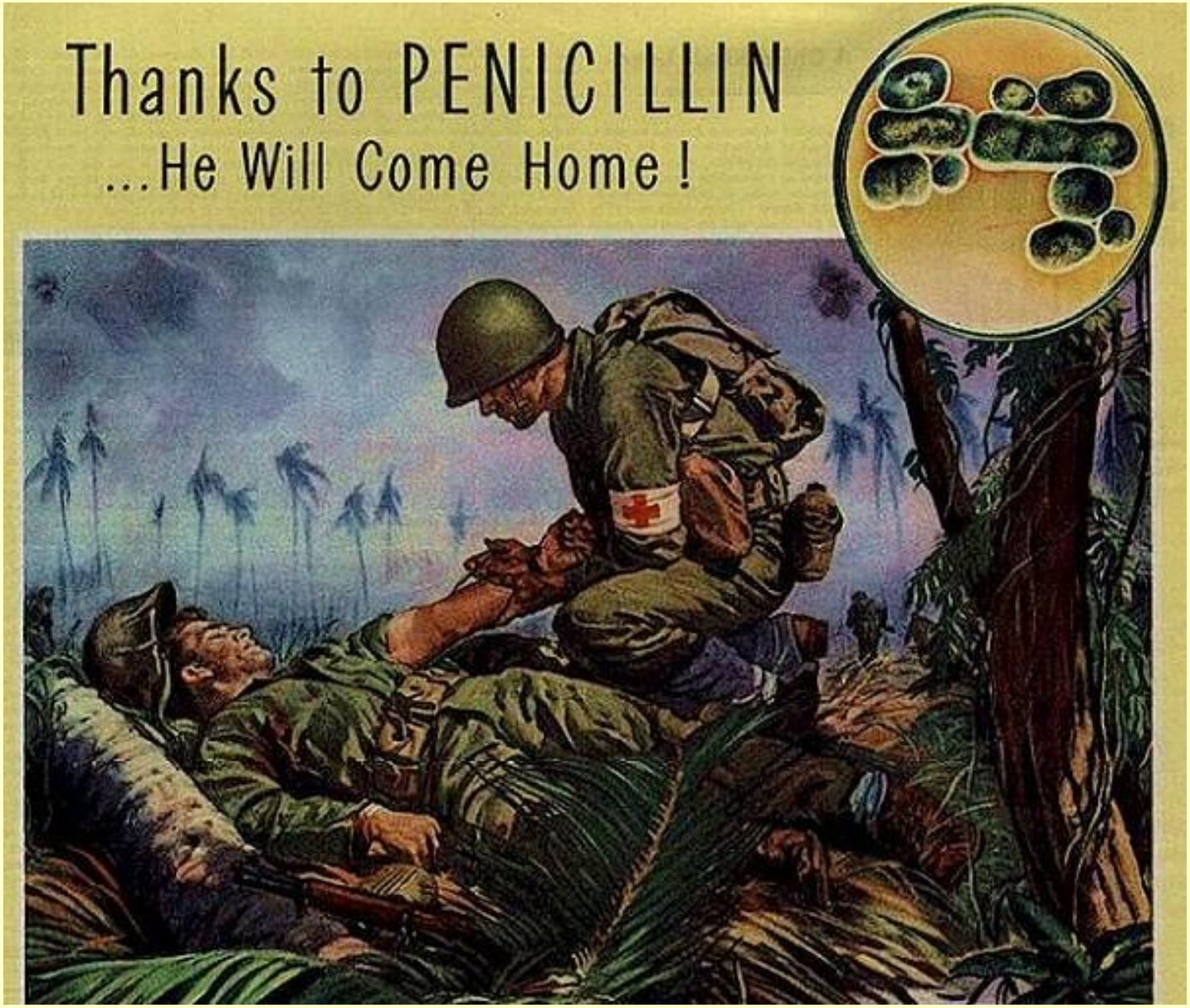
Gerhard Domagk

1940

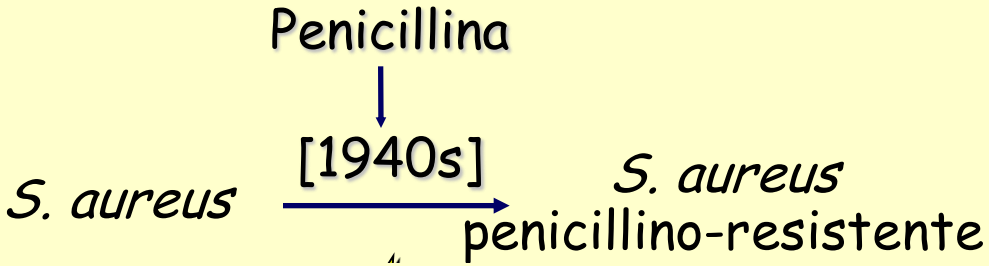
Ernst Boris Chain e Howard Walter Florey

Thanks to PENICILLIN

...He Will Come Home!

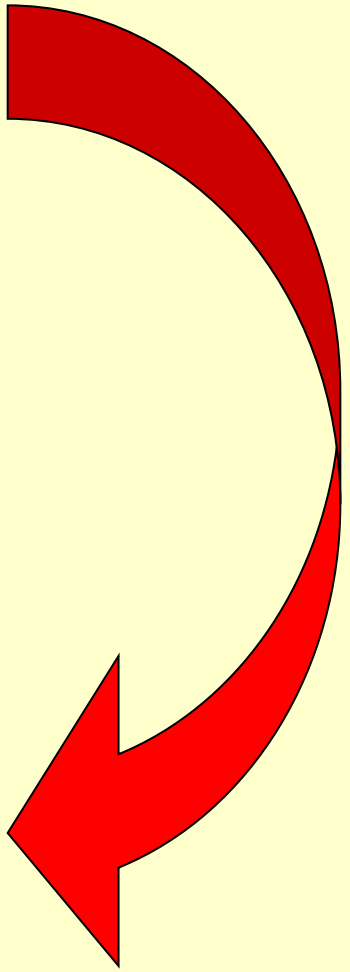


Evoluzione della resistenza nei cocchi Gram positivi

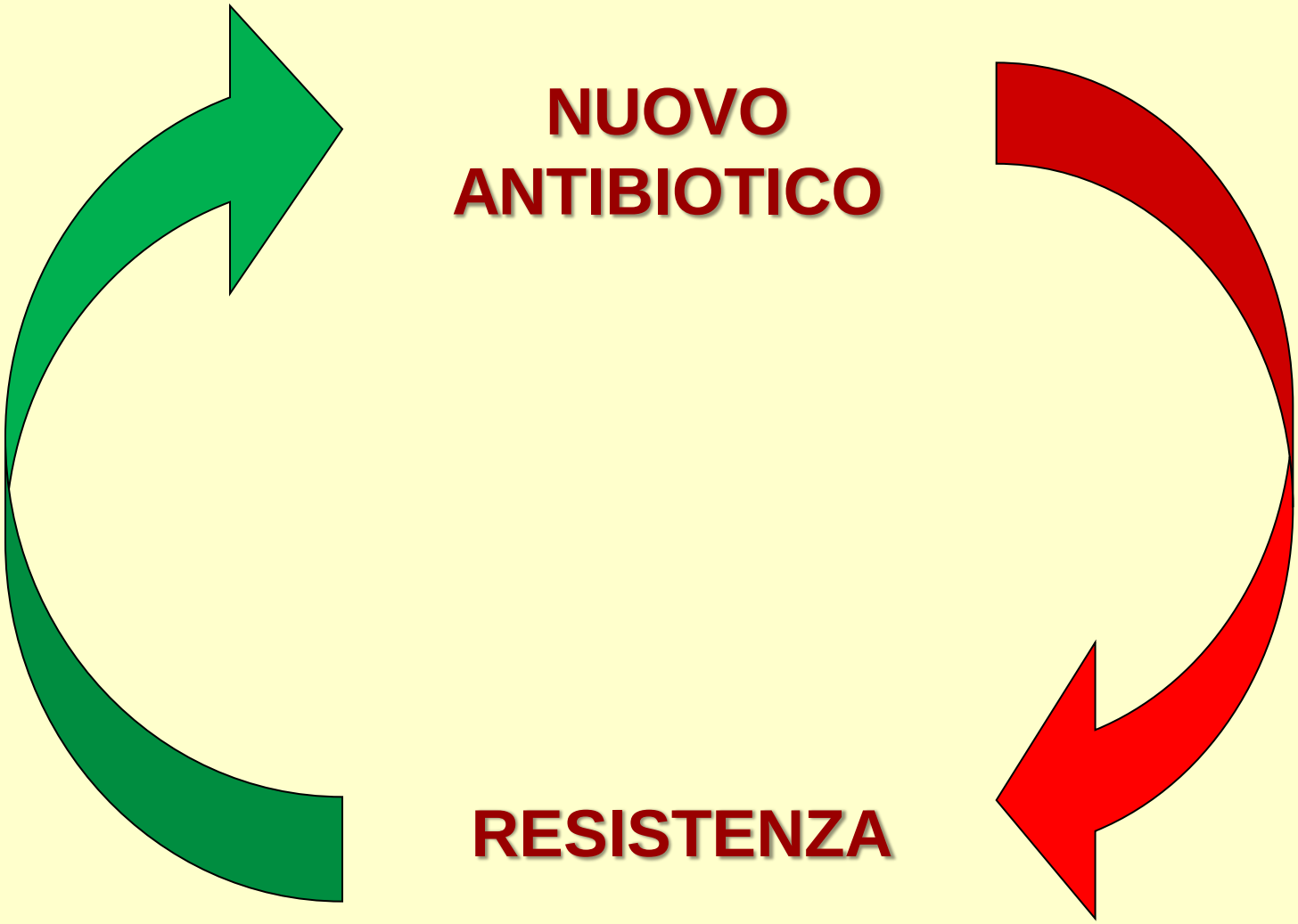


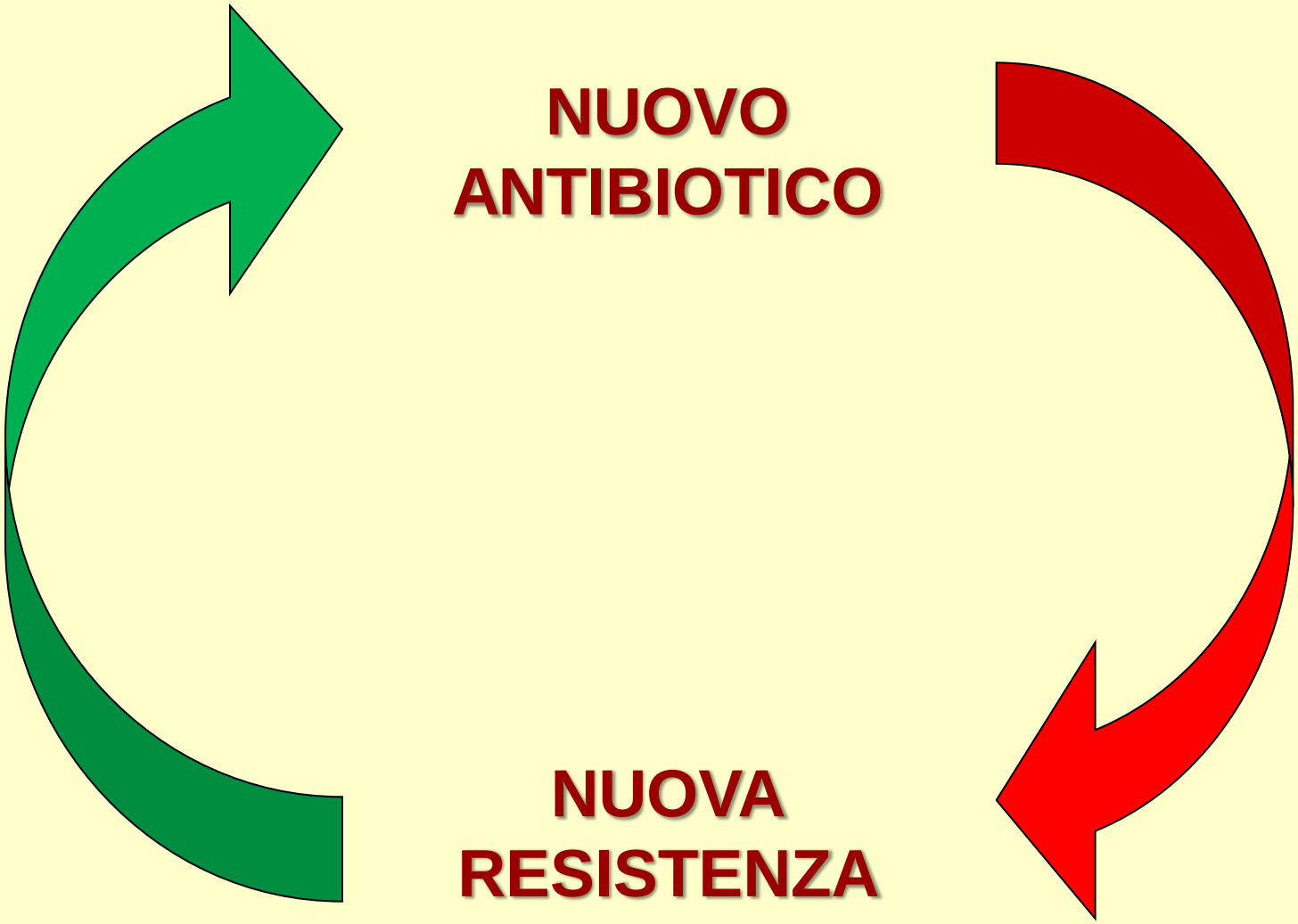
CDC, Prevent Antimicrobial Resistance, Aprile 2002

ANTIBIOTICO

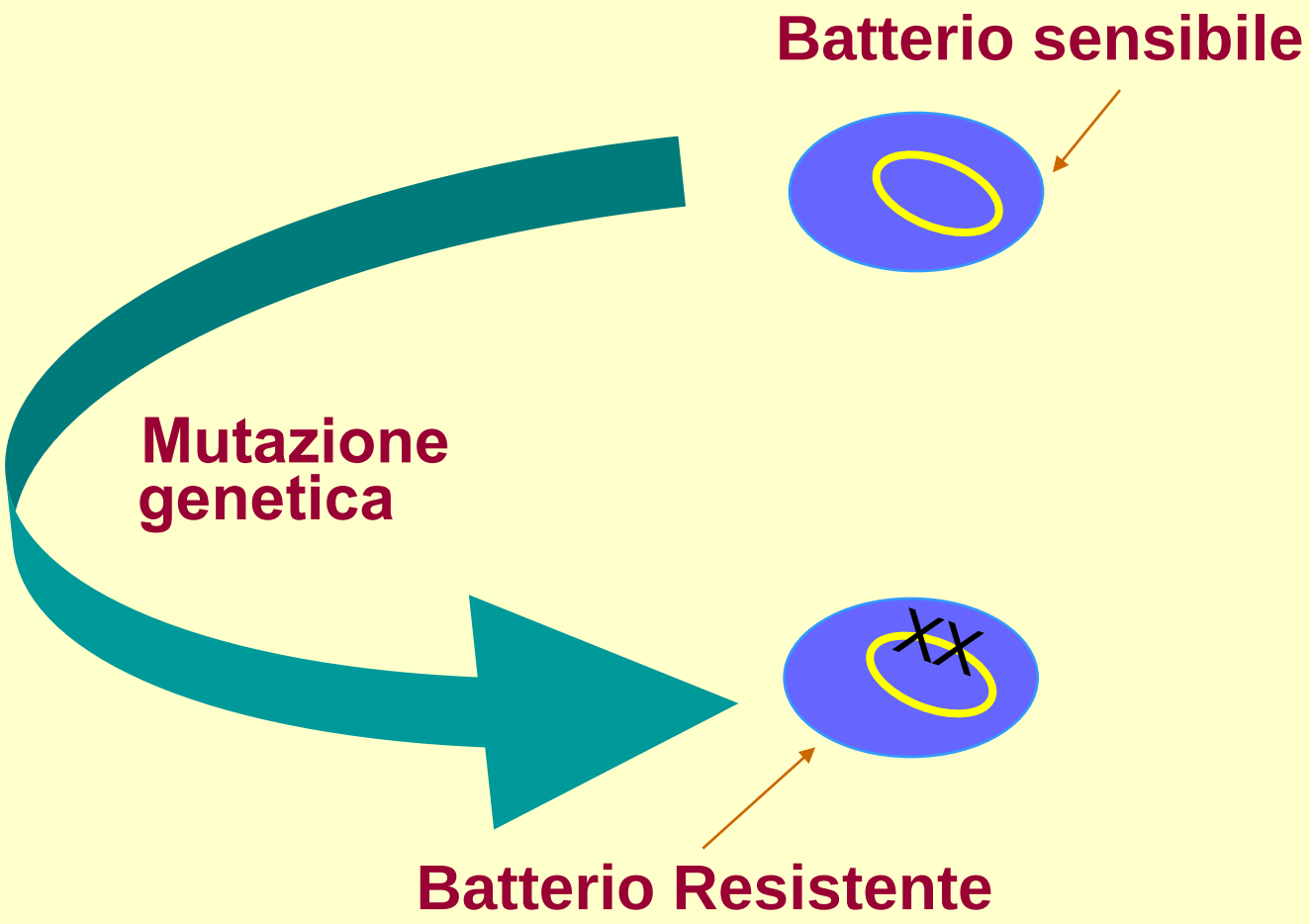


RESISTENZA

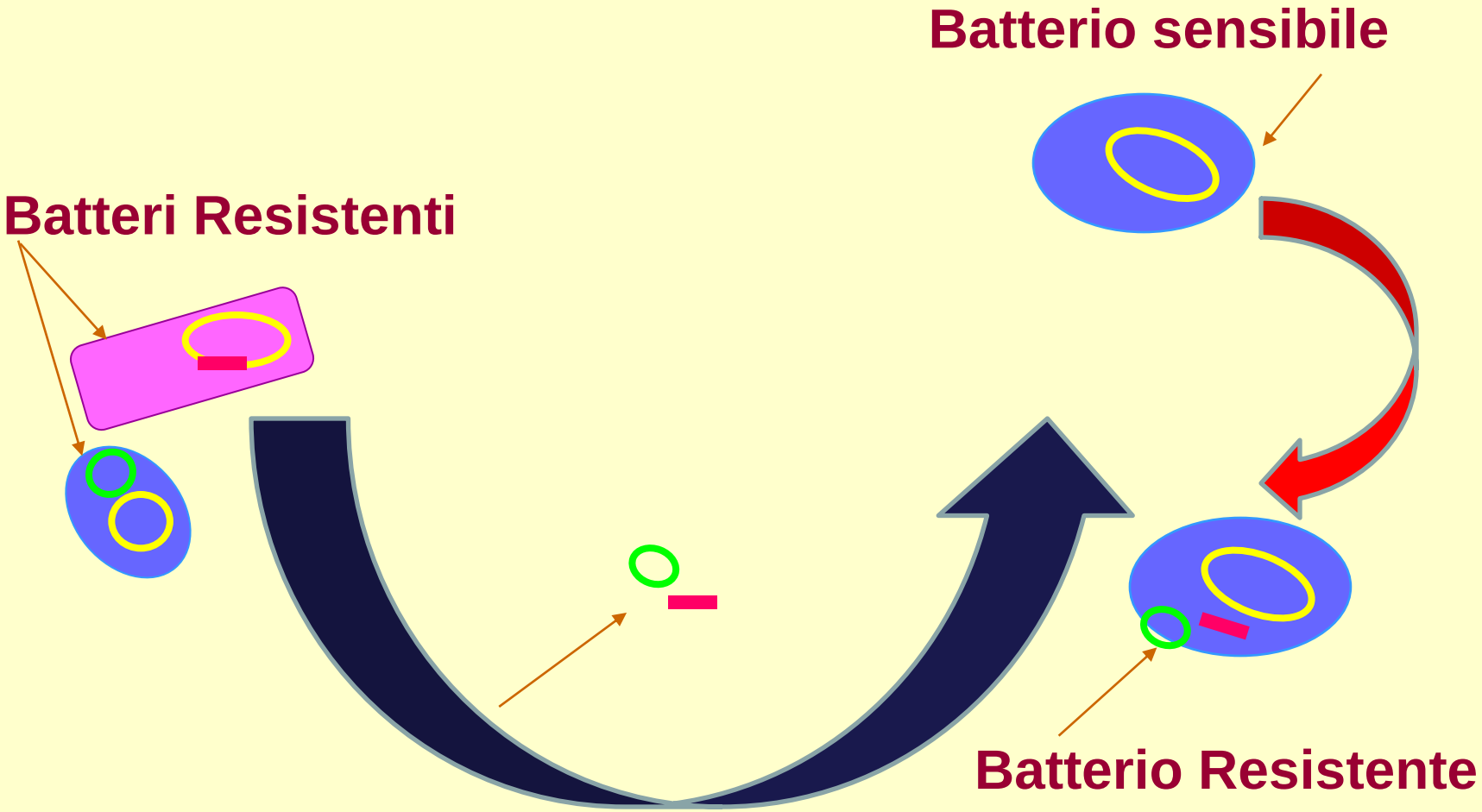

NUOVO
ANTIBIOTICO
RESISTENZA


NUOVO
ANTIBIOTICO
NUOVA
RESISTENZA

Come compare l'antibioticoresistenza



Come compare l'antibioticoresistenza

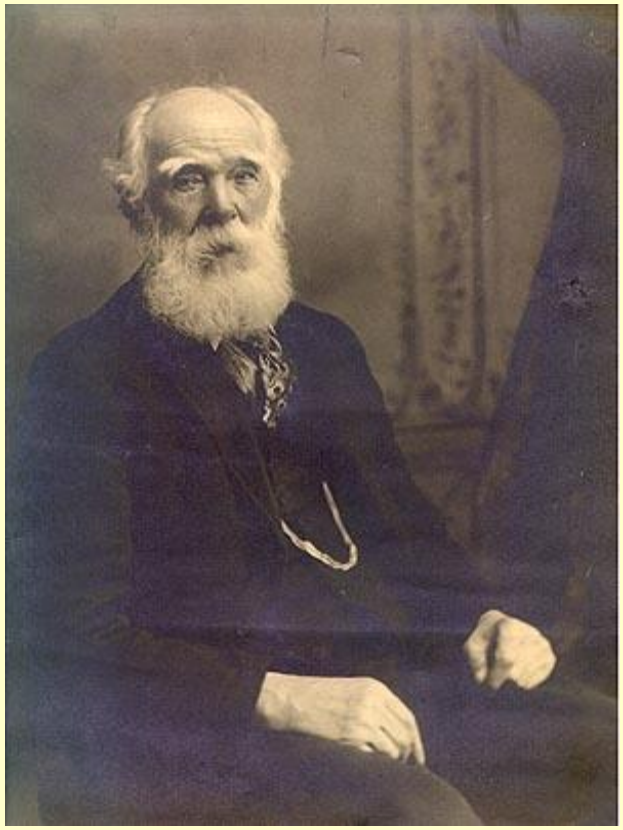


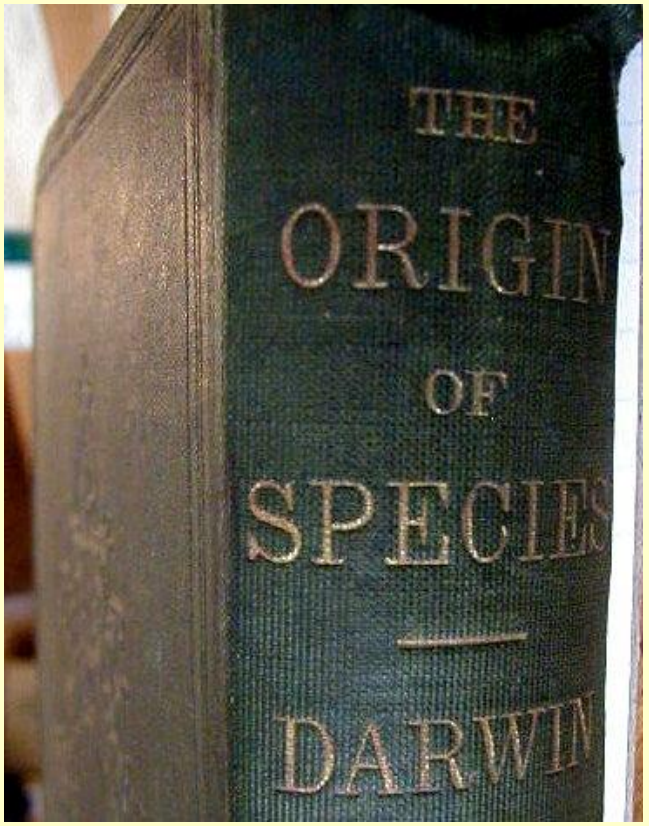
La resistenza agli antibiotici è un fenomeno naturale

Antibiotico resistenza nei batteri isolati dalle feci di pinguini in Antartide.

Can J Microbiol. 2009 Jan;55(1):37-45.

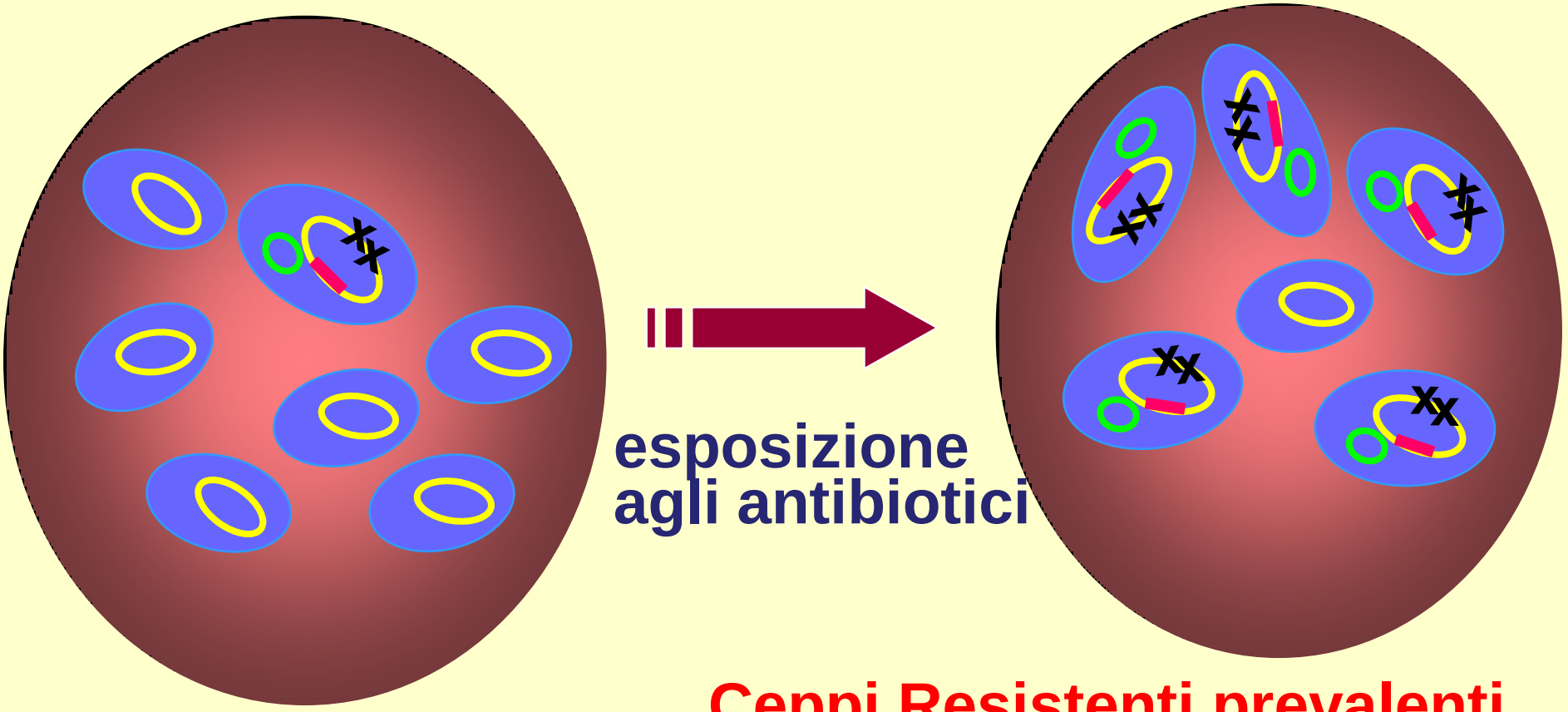
Selezione ed espansione dei ceppi Resistenti





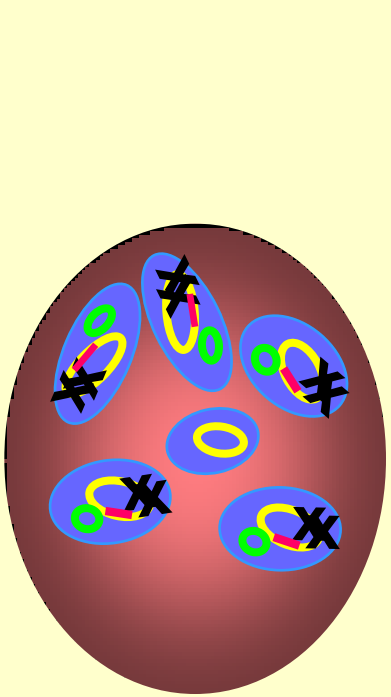
Selezione ed espansione dei ceppi Resistenti

Ceppi Resistenti rari

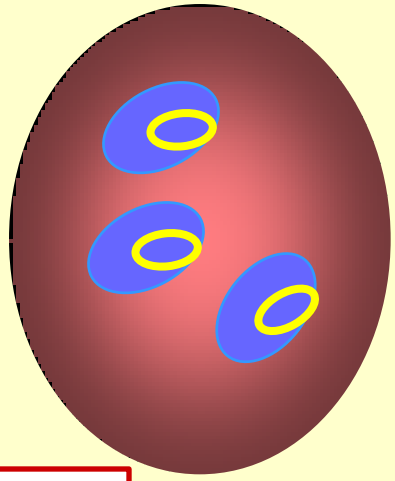


Ceppi Resistenti prevalenti

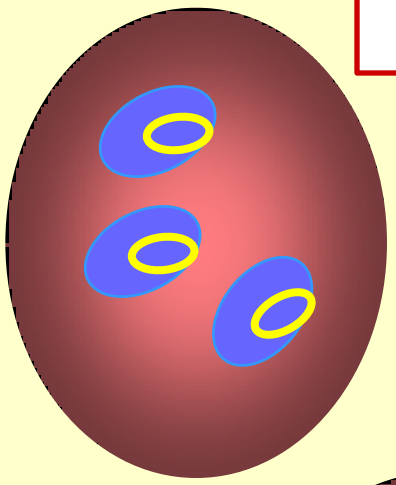
Diffusione dei ceppi Resistenti



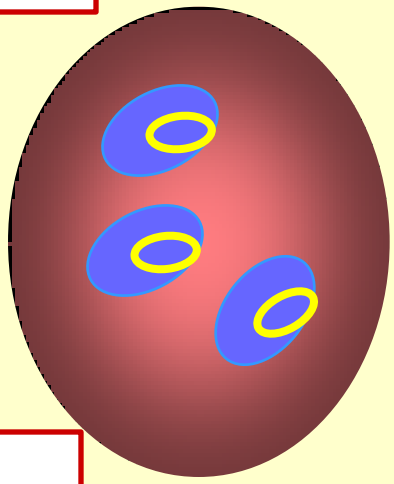
Paolo



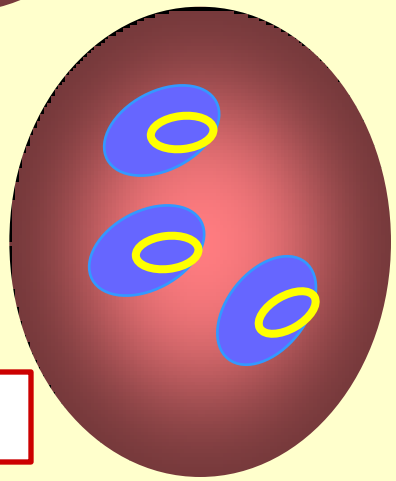
Luca



Renzo

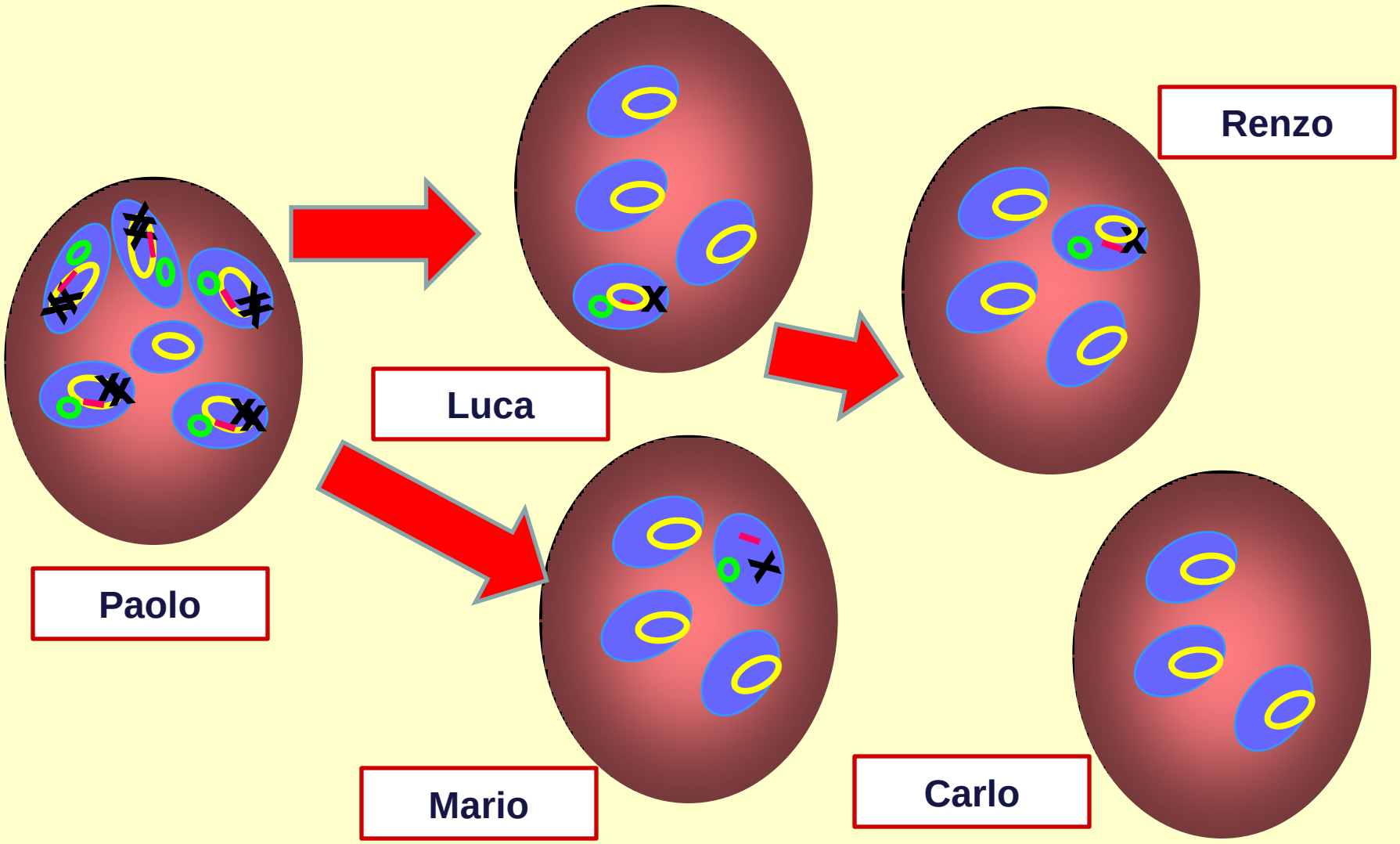


Mario



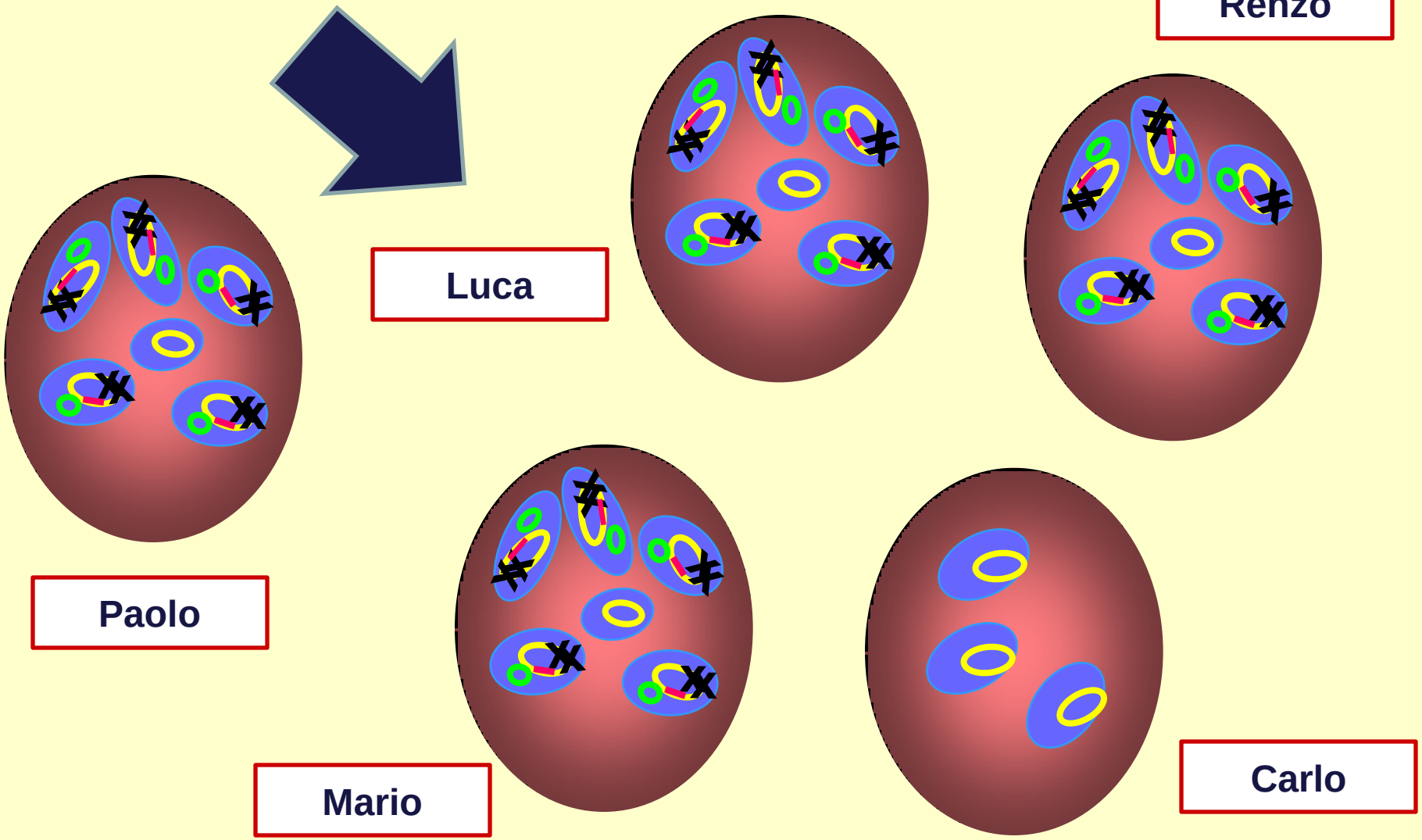
Carlo

Diffusione dei ceppi Resistenti



Diffusione dei ceppi Resistenti

esposizione agli antibiotici



Meccanismi di antibioticoresistenza

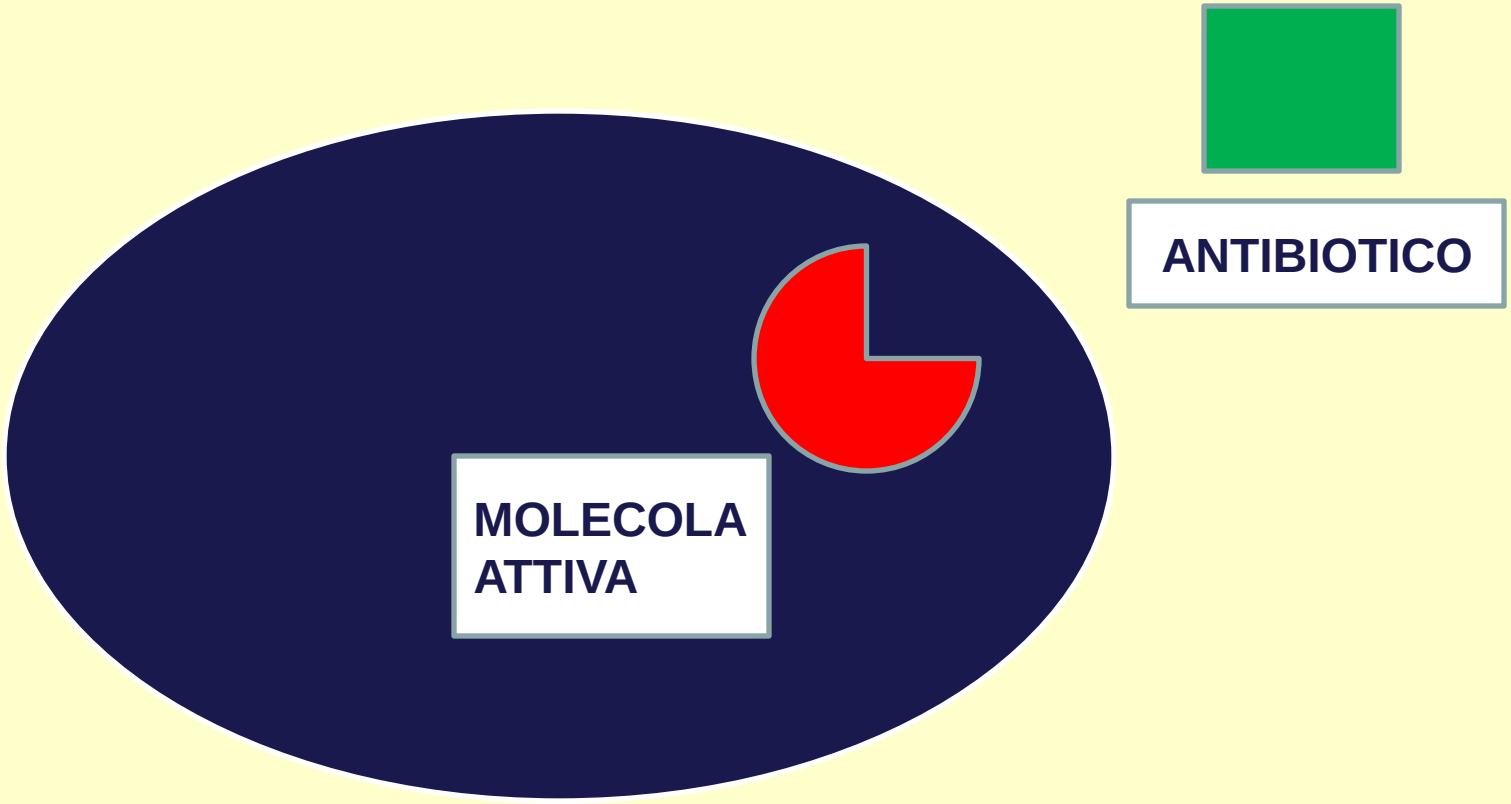
Modificazione del bersaglio

Diminuzione della permeabilità

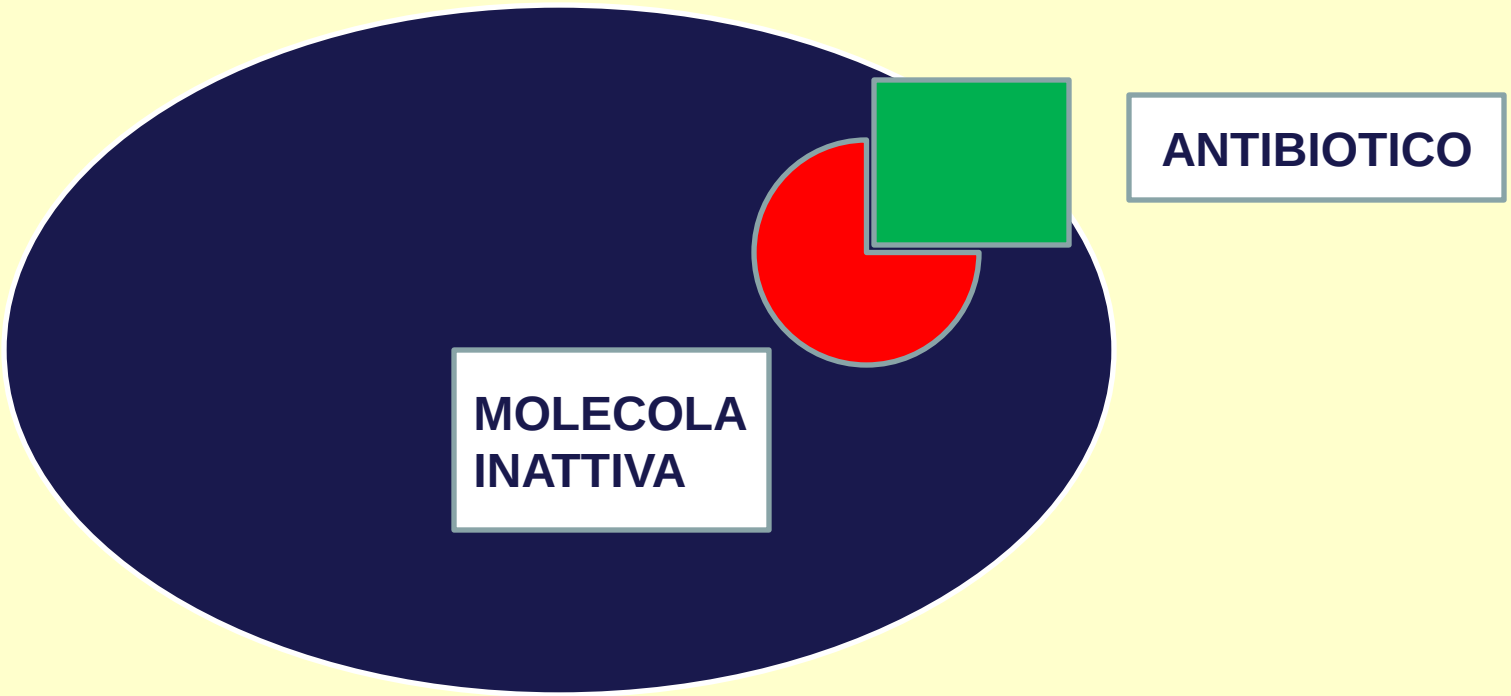
Espulsione dell'antibiotico

Inattivazione dell'antibiotico

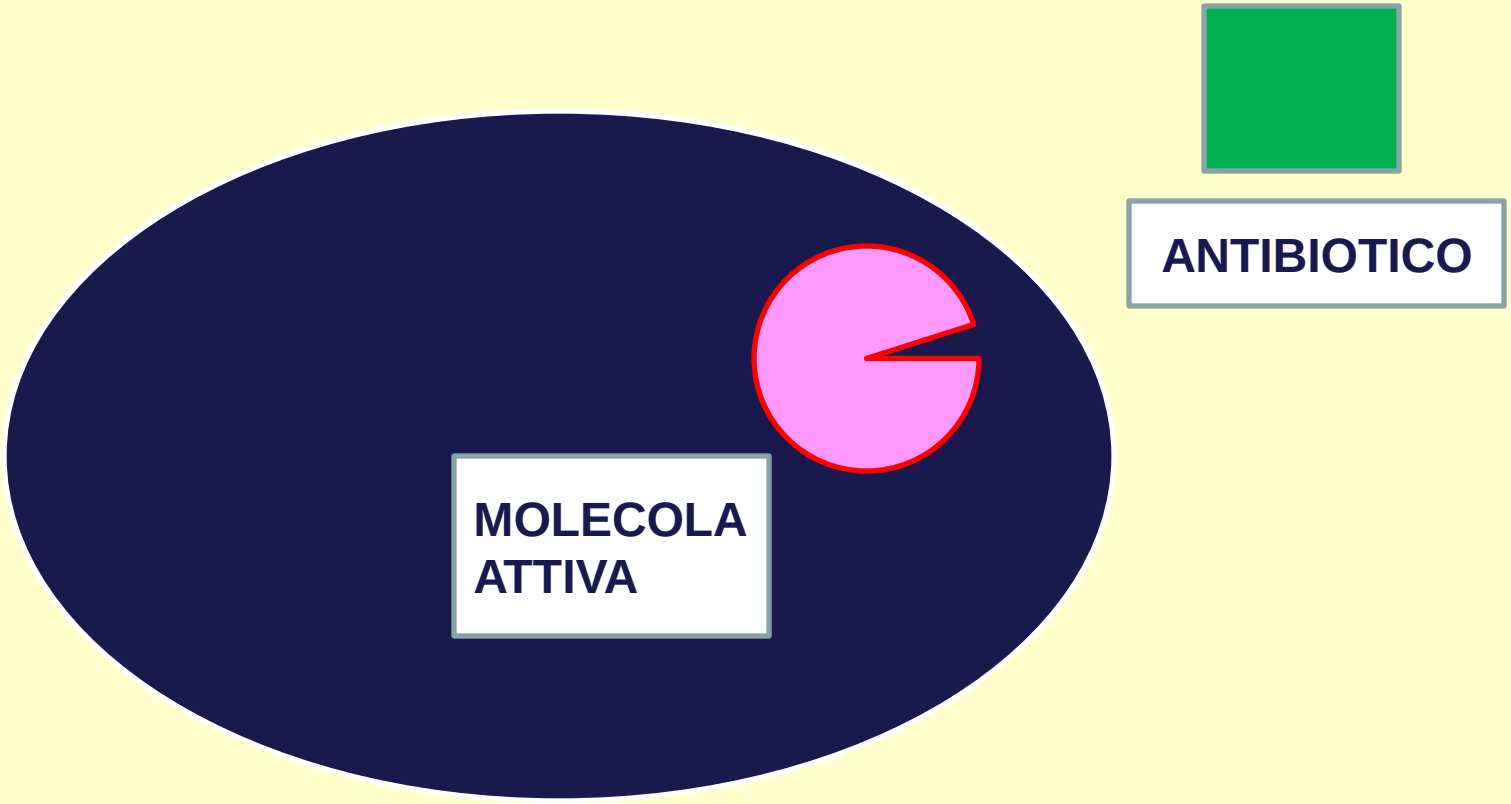
Meccanismi di antibioticoresistenza 1



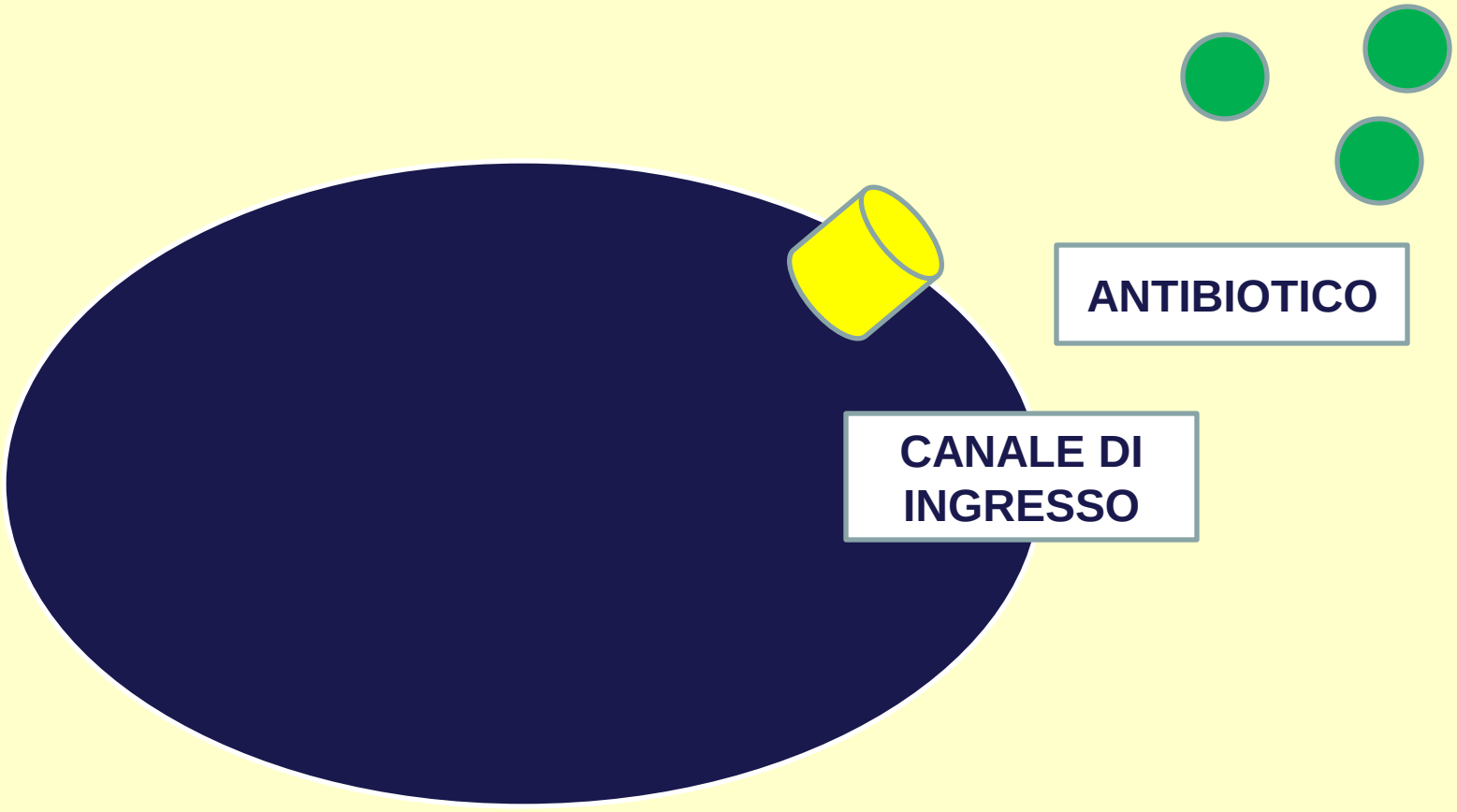
Meccanismi di antibioticoresistenza 1



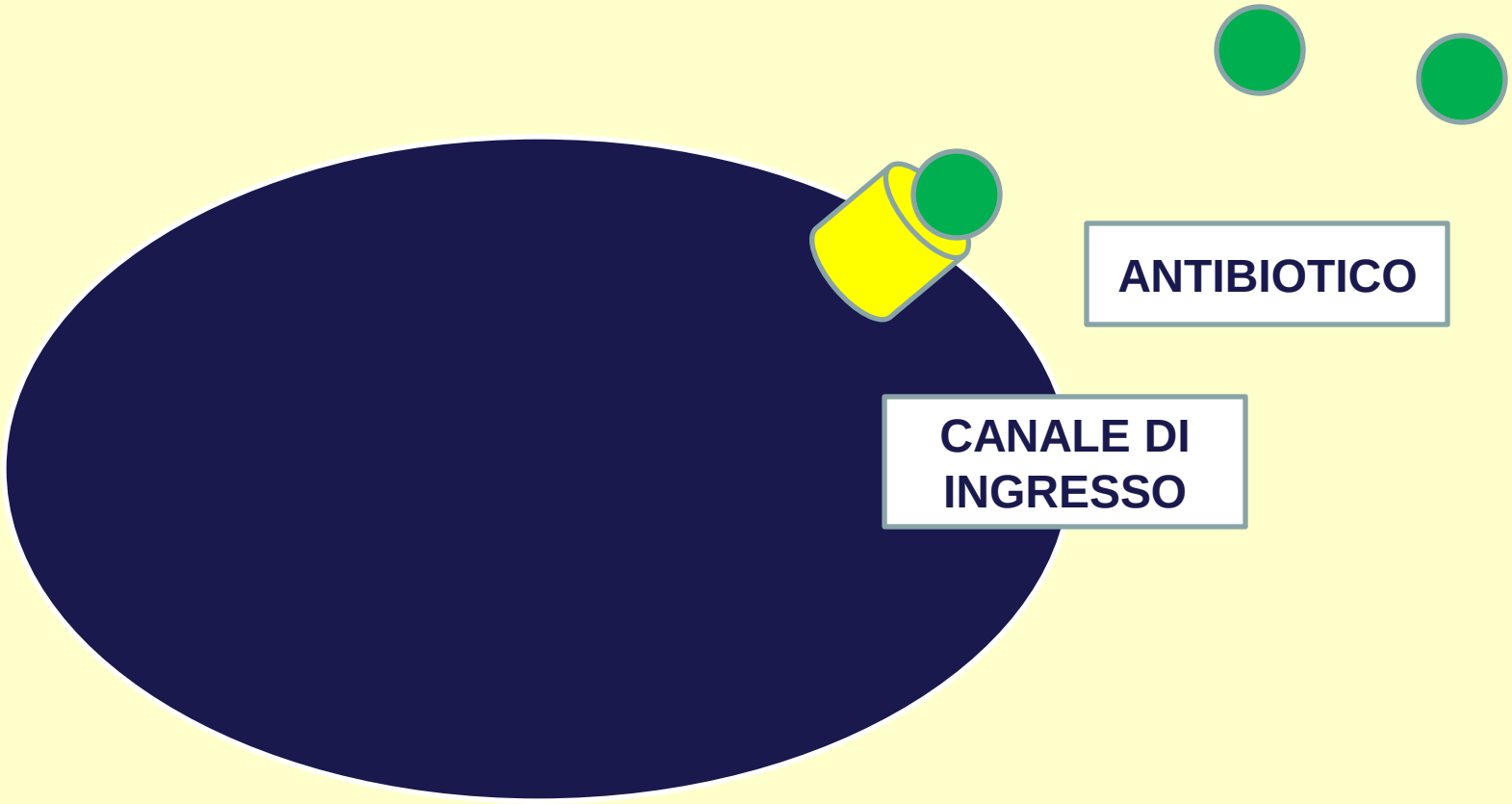
Modificazione del bersaglio



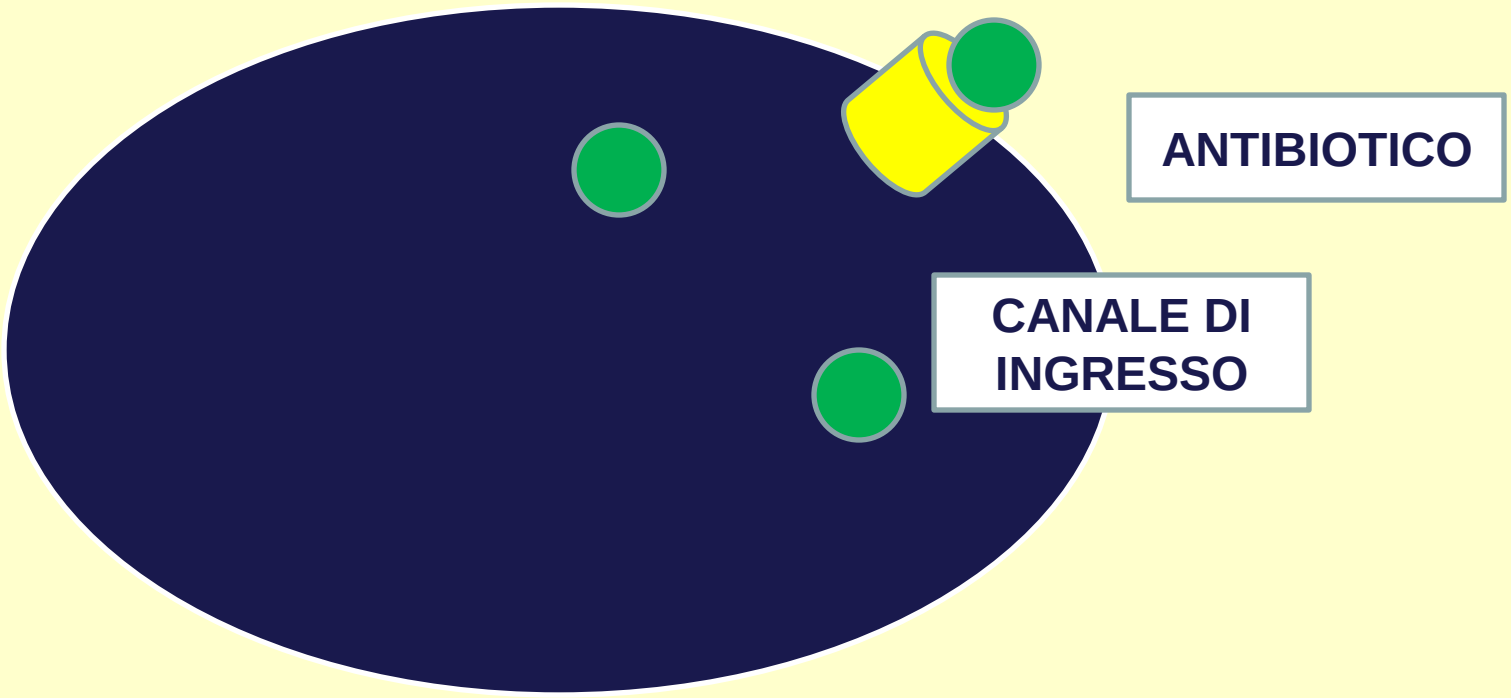
Meccanismi di antibioticoresistenza 2



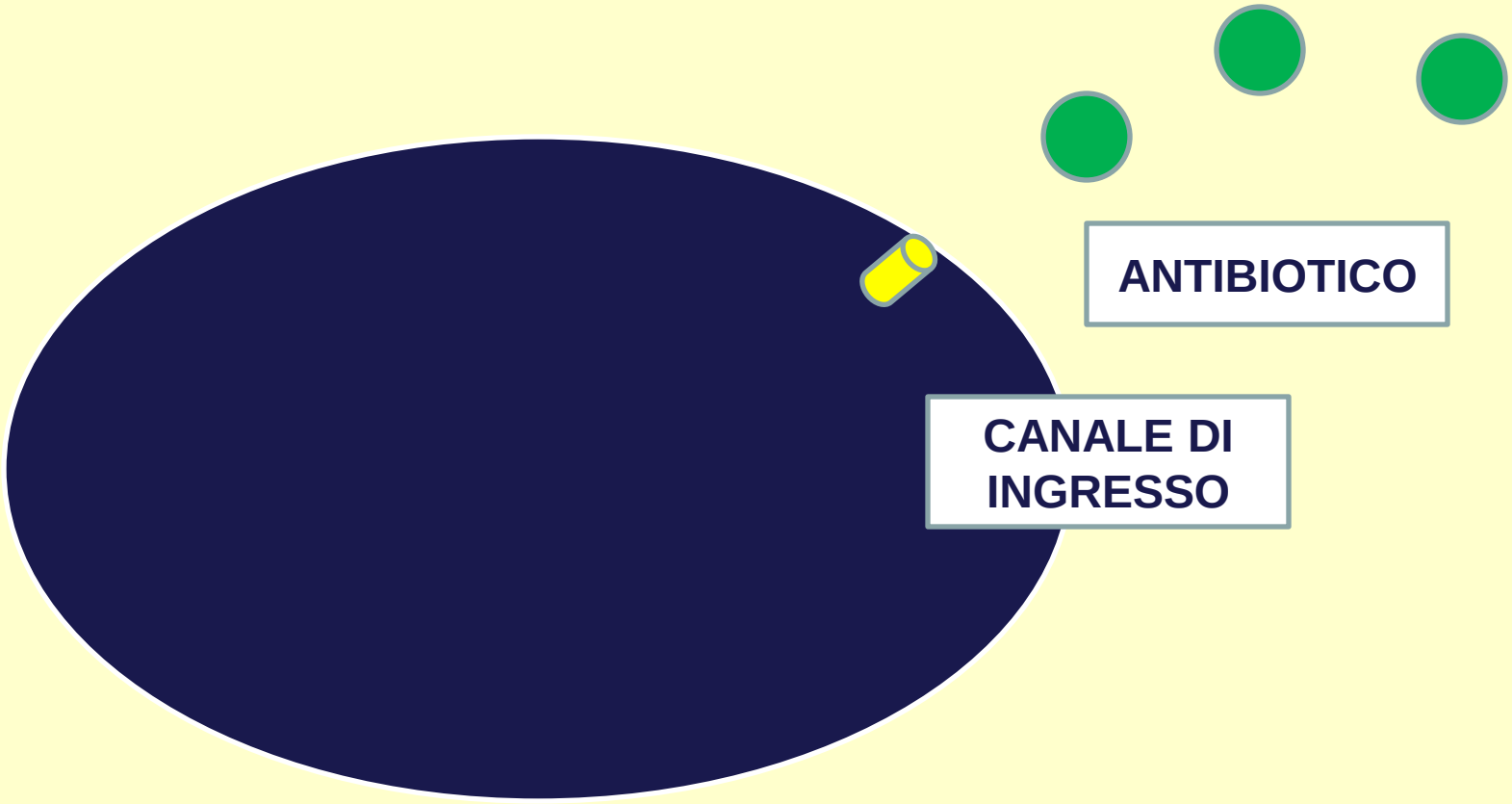
Meccanismi di antibioticoresistenza 2



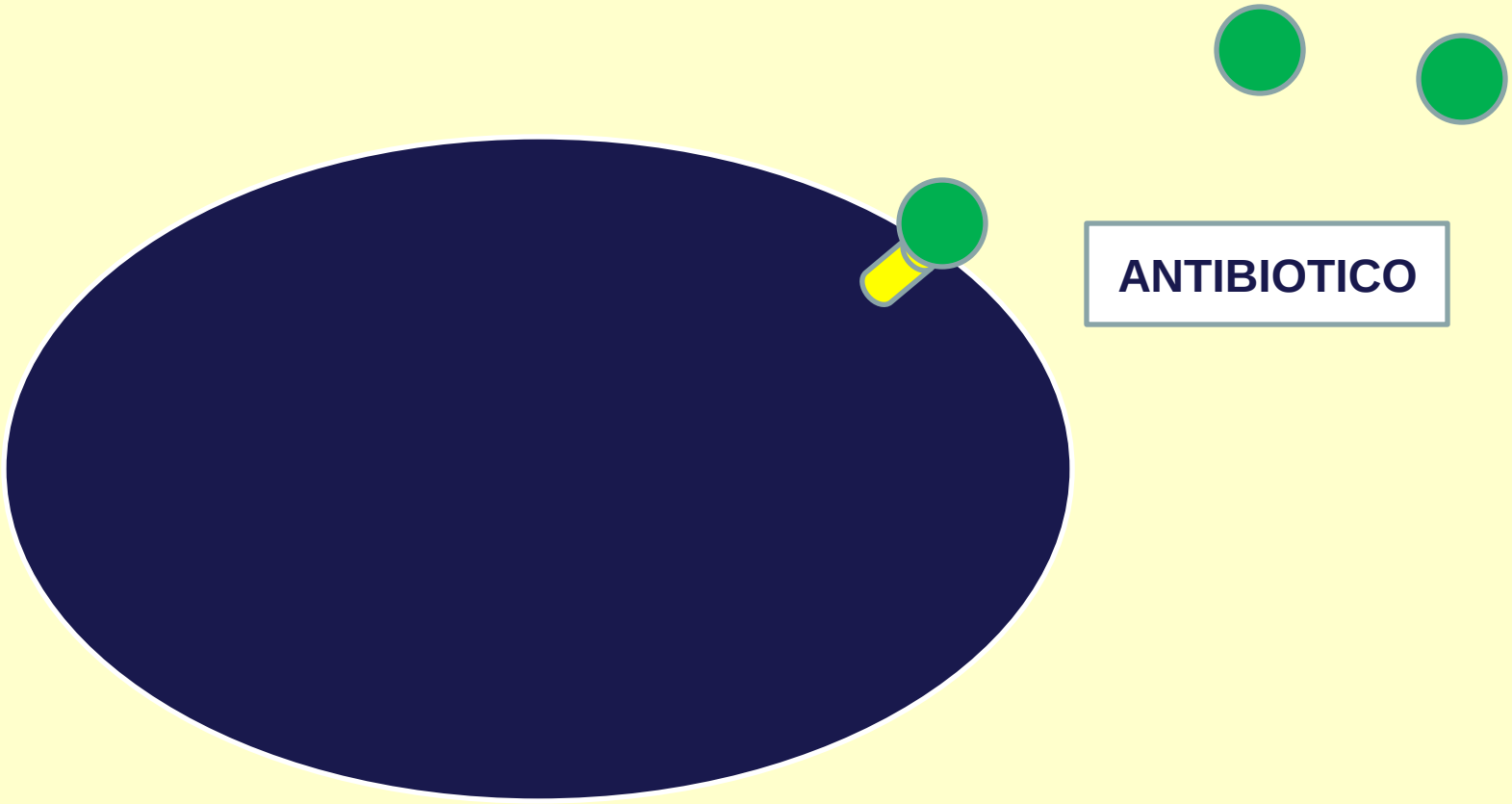
Meccanismi di antibioticoresistenza 2



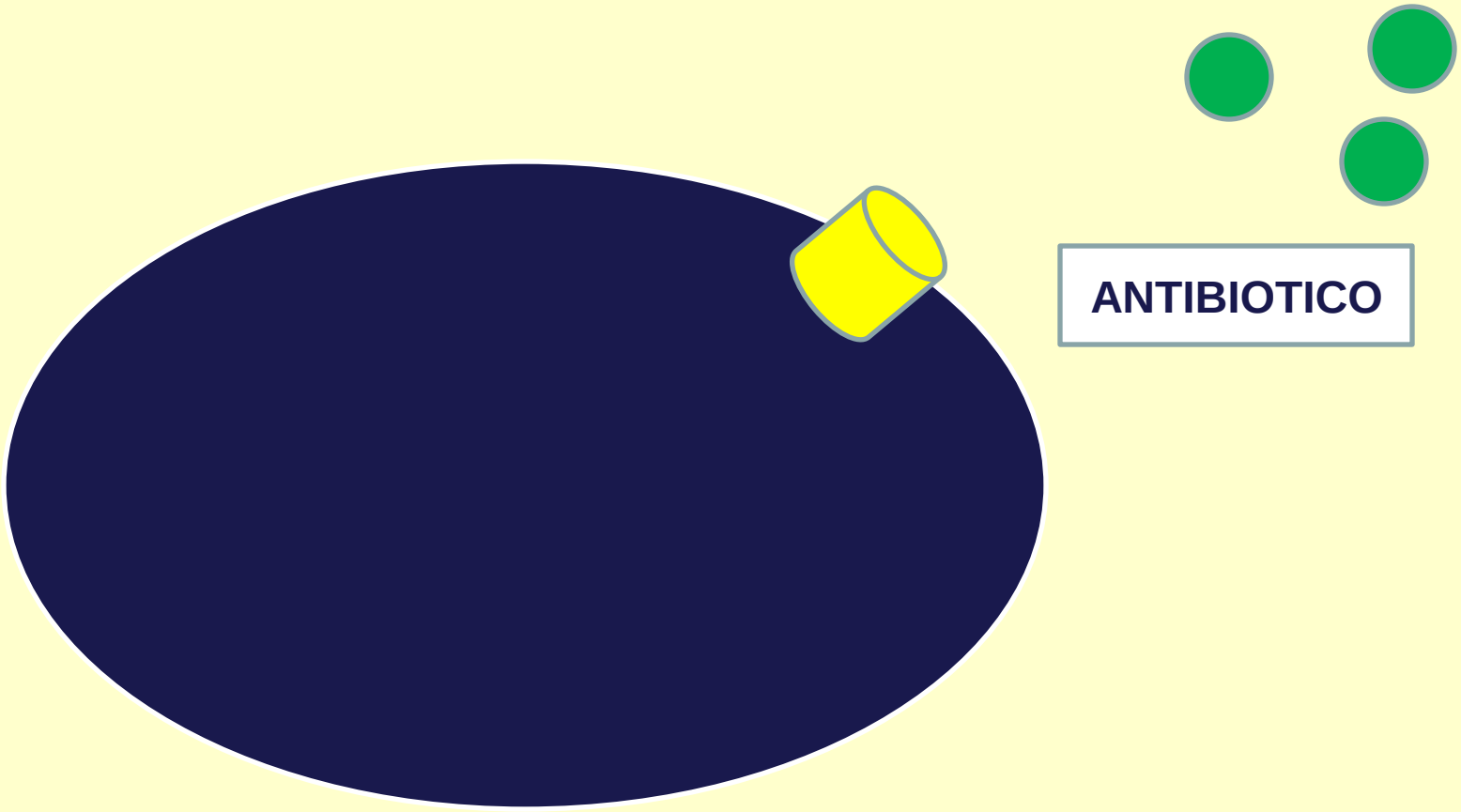
Meccanismi di antibioticoresistenza 2



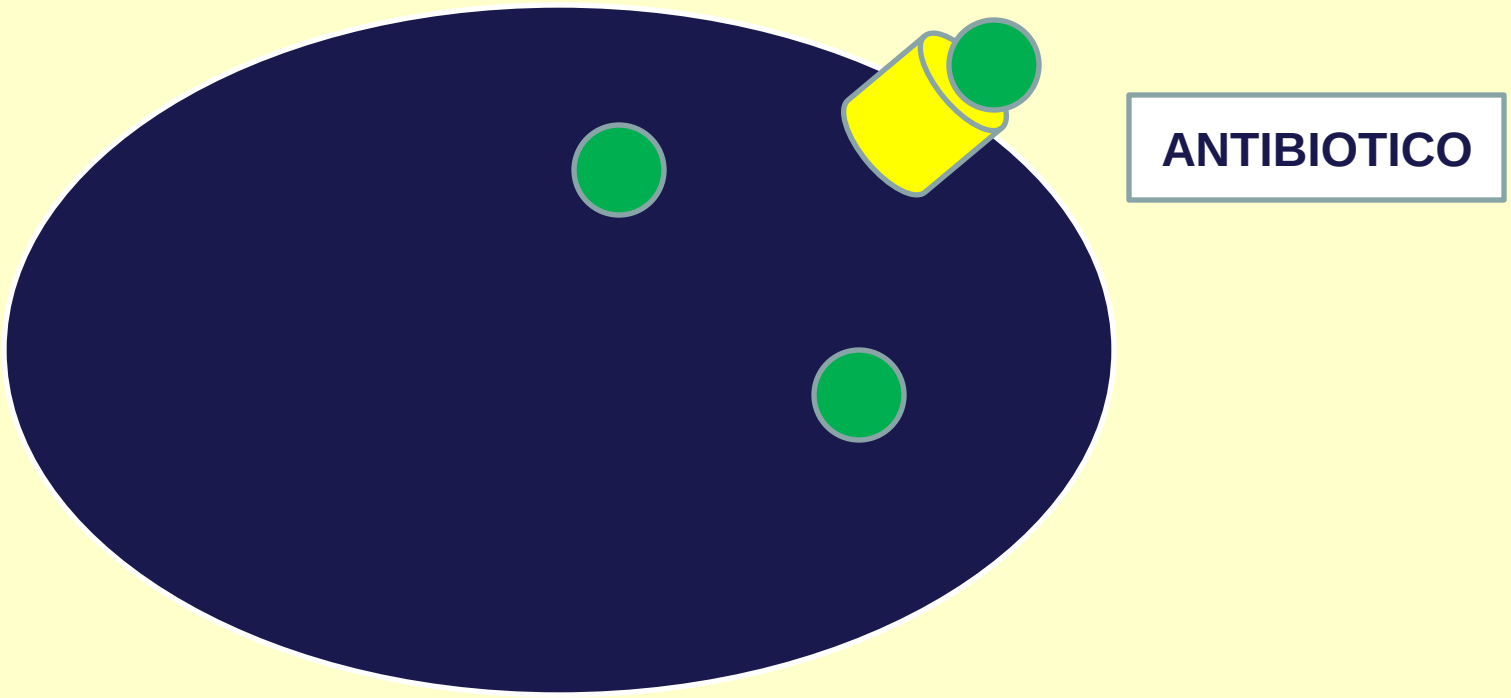
Diminuzione della permeabilità



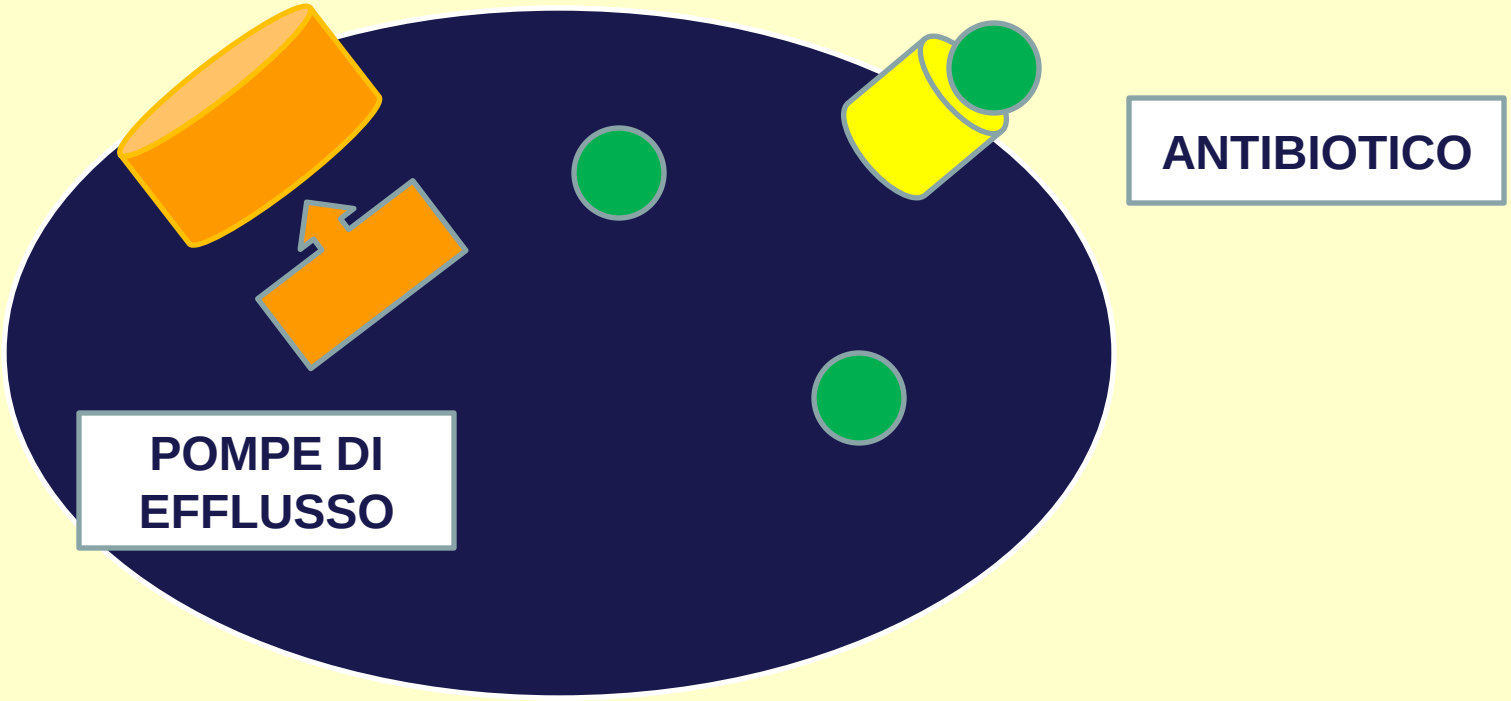
Meccanismi di antibioticoresistenza



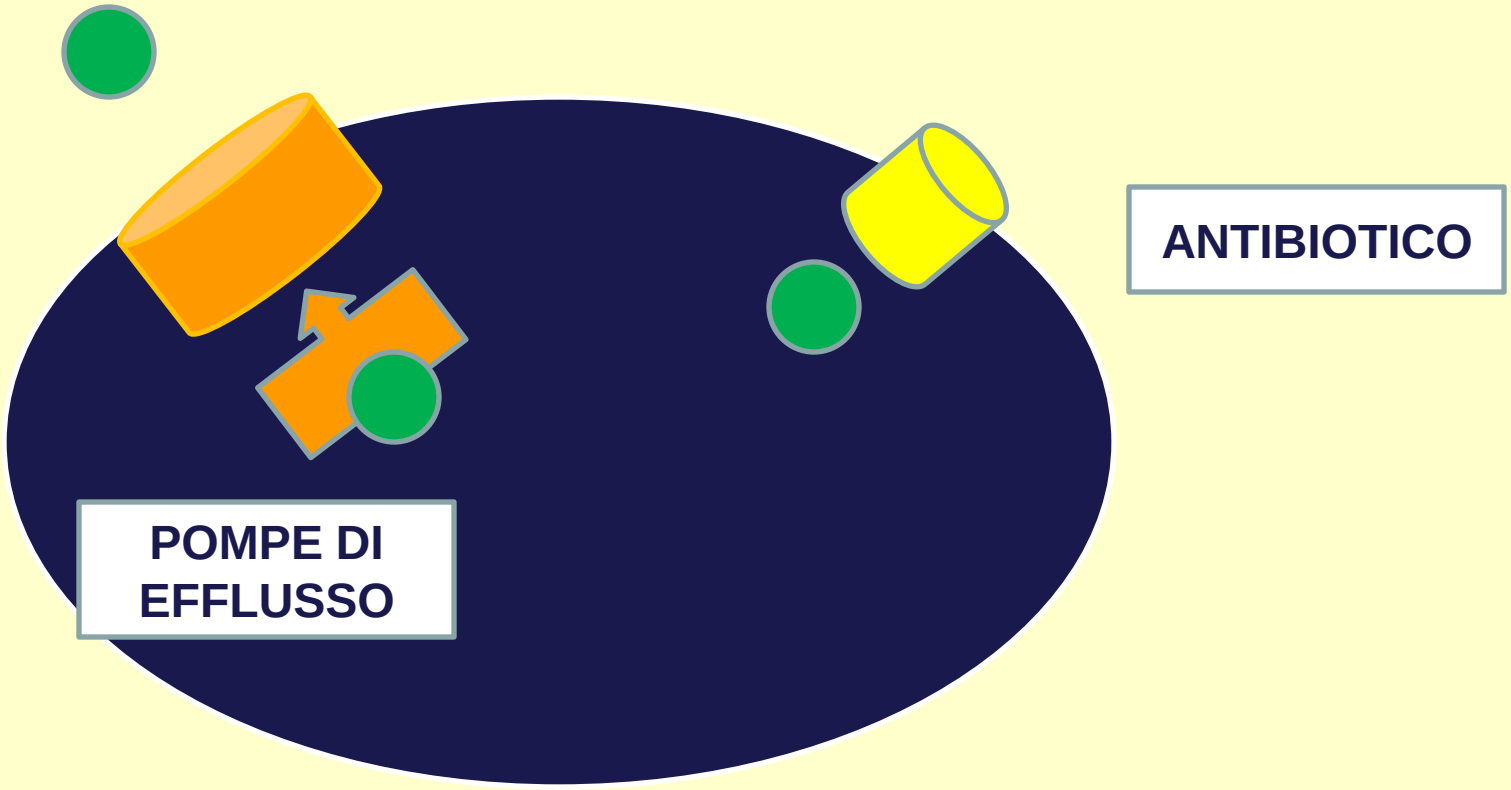
Meccanismi di antibioticoresistenza 3



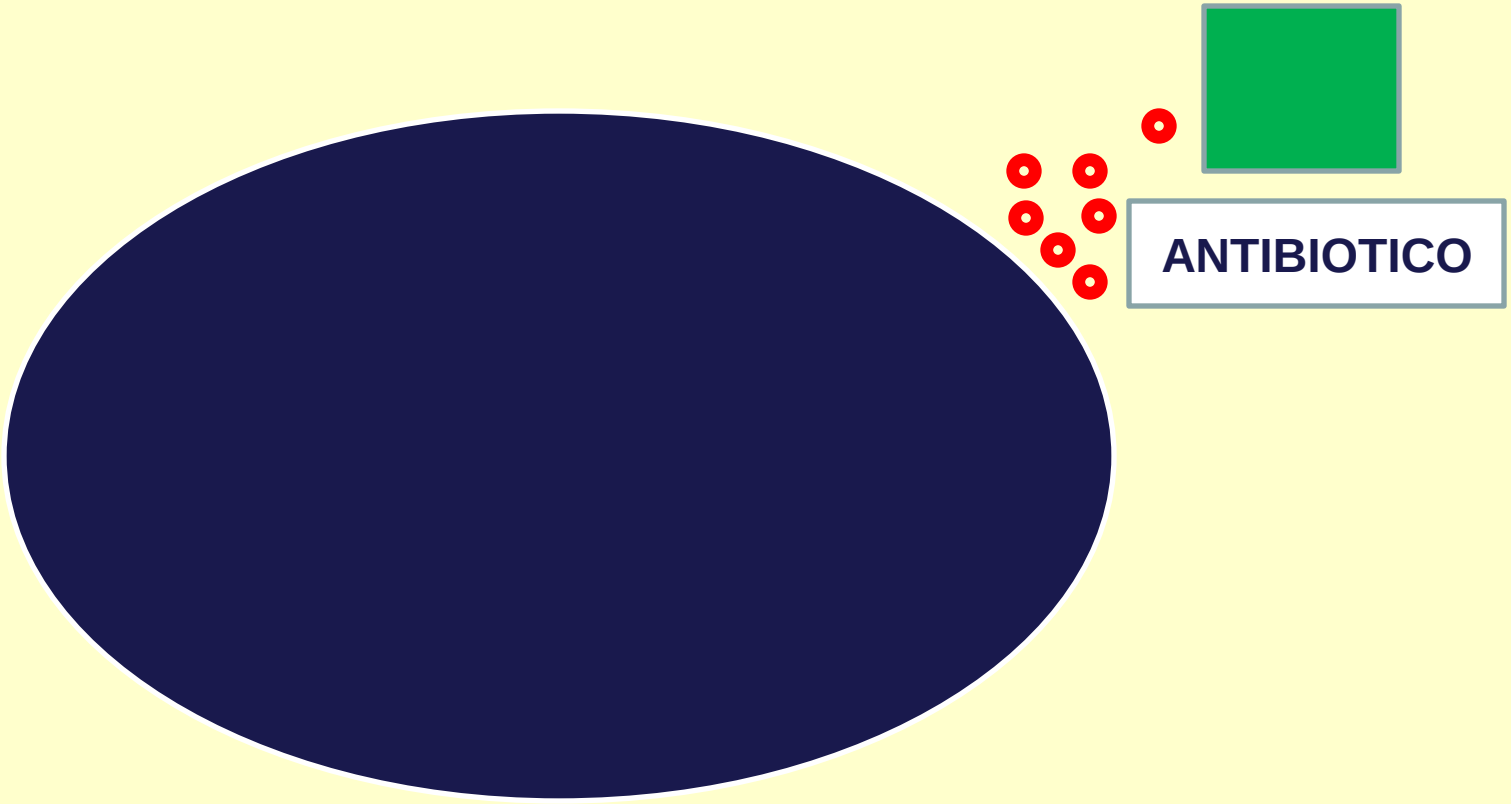
Meccanismi di antibioticoresistenza 3



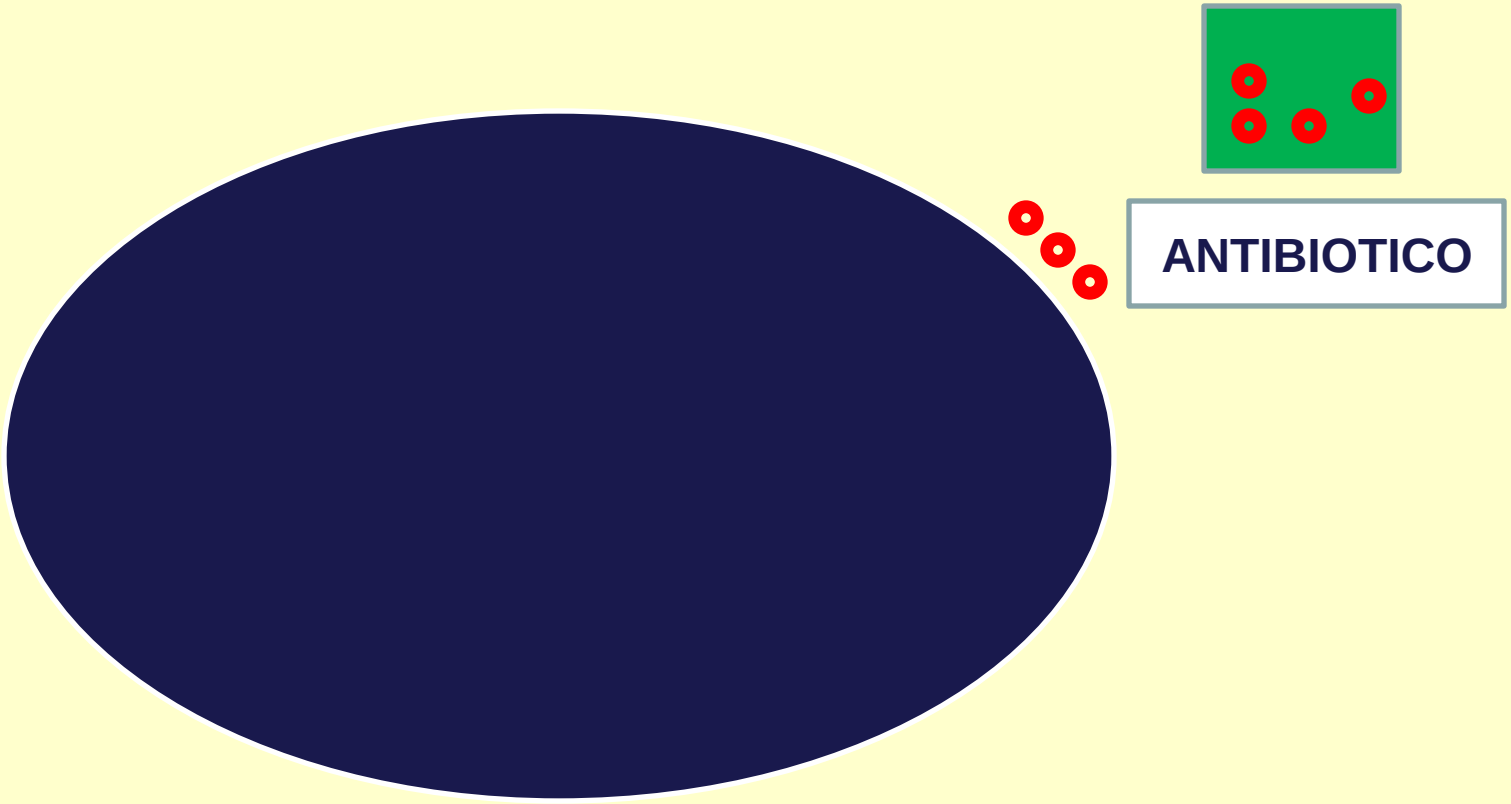
Espulsione dell'antibiotico



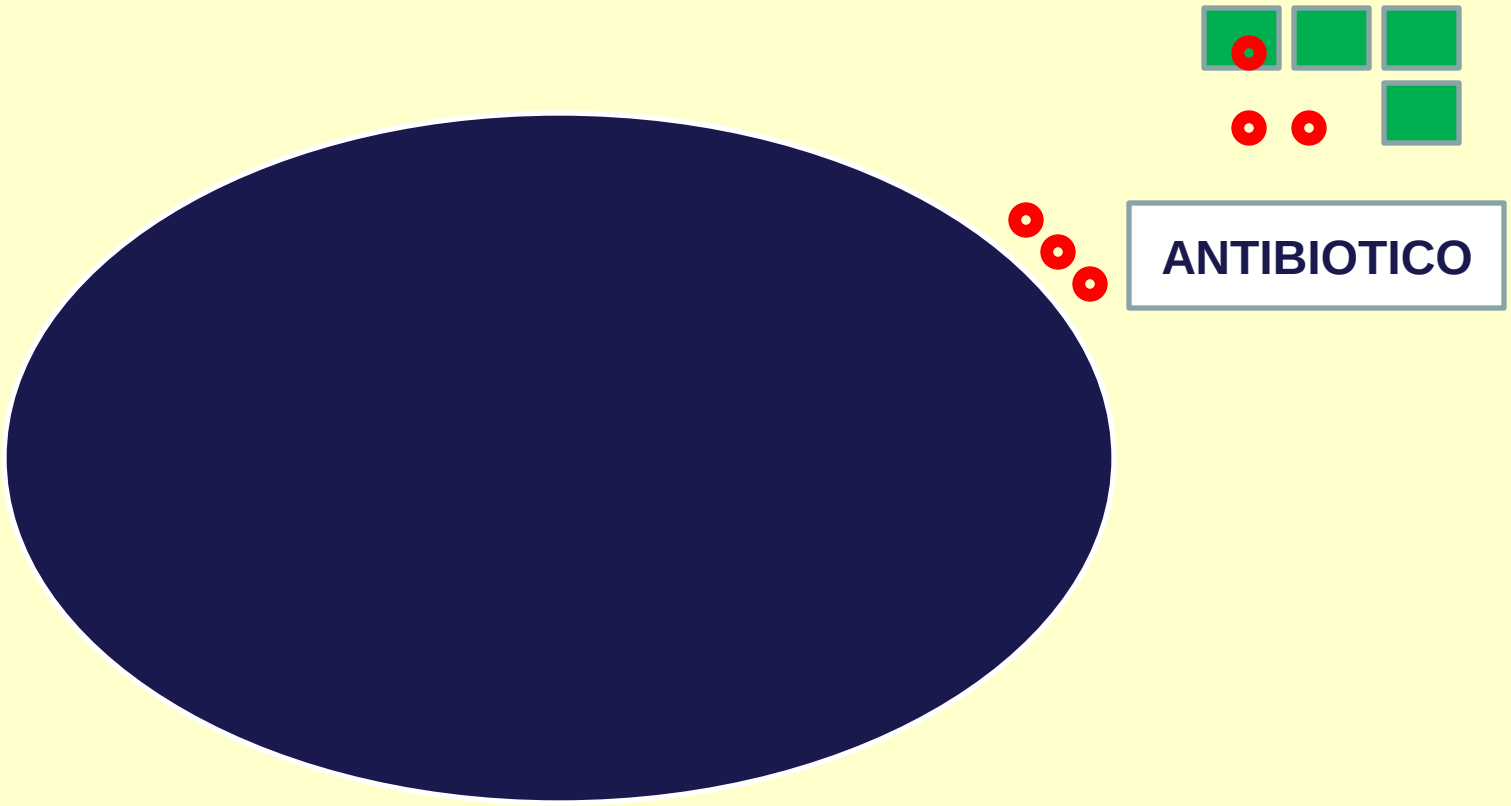
Meccanismi di antibioticoresistenza 4



Meccanismi di antibioticoresistenza 4



Inattivazione dell'antibiotico



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225-2012

Agenzia sanitaria e sociale regionale

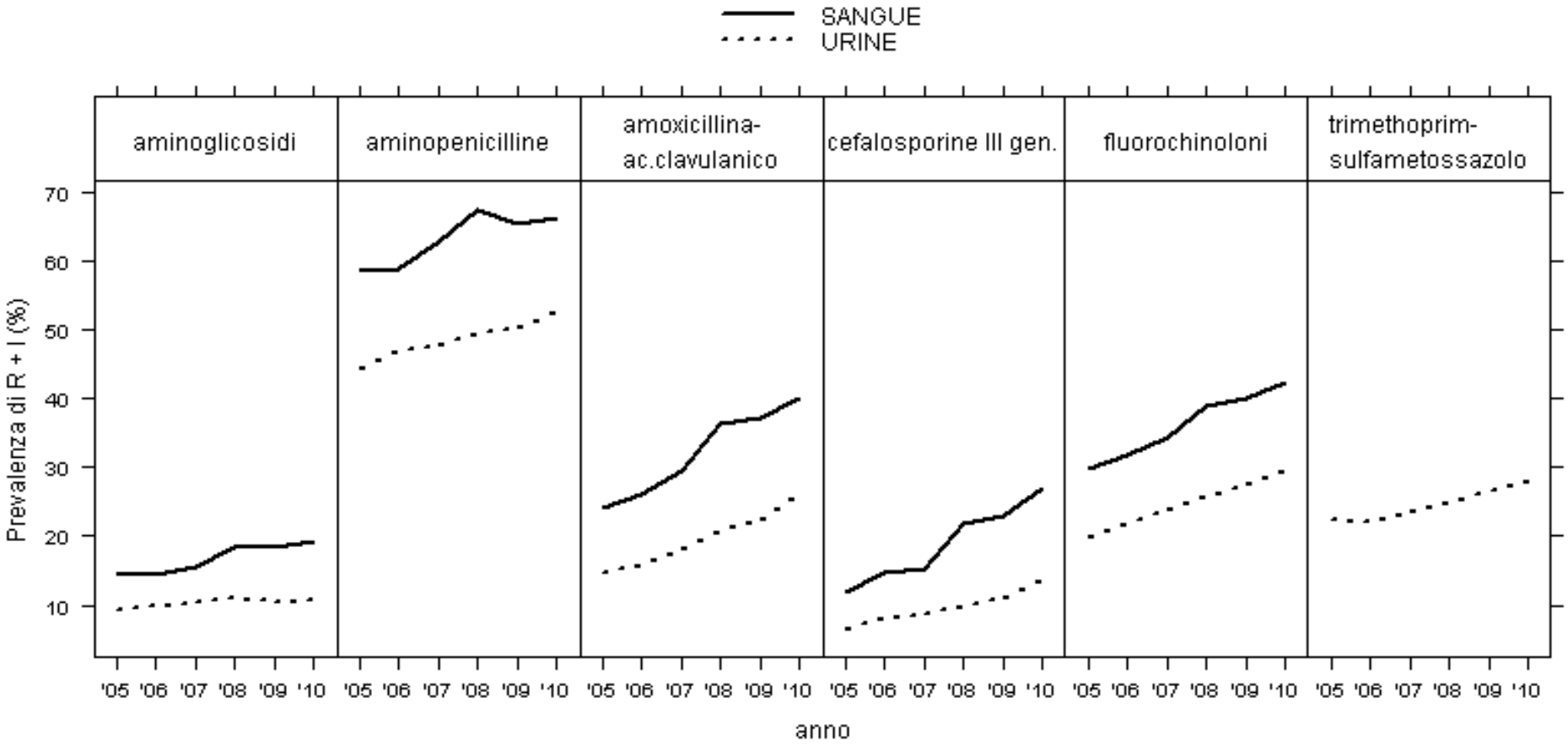
RegioneEmiliaRomagna
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

Sorveglianza dell'antibioticoresistenza e uso di antibiotici sistemici in Emilia-Romagna

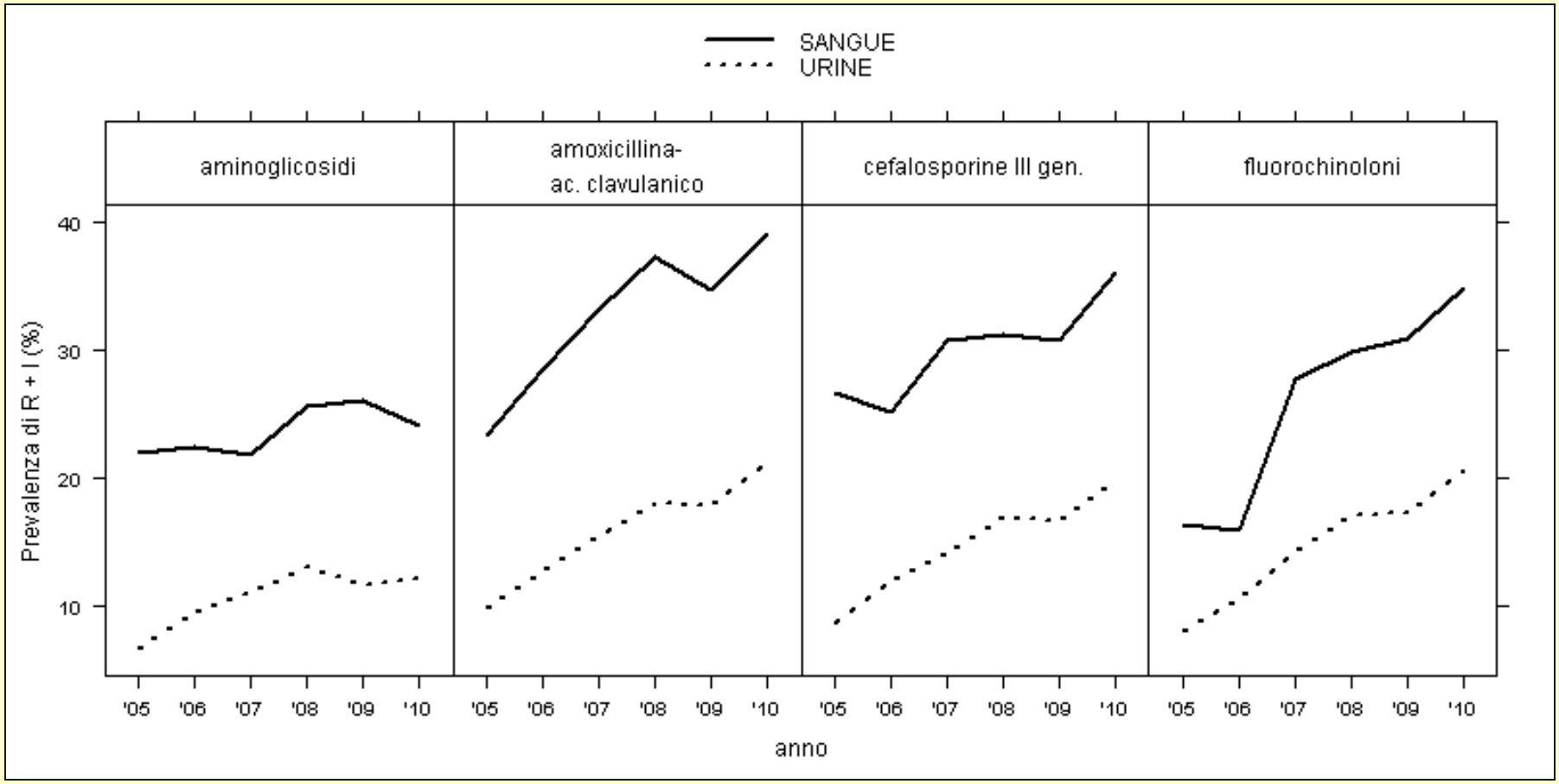
Rapporto 2010

Rischio infettivo

Antibioticoresistenze di E. coli



Antibioticoresistenze di K. pneumoniae



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Modena

OSSERVATORIO MICROBIOLOGICO

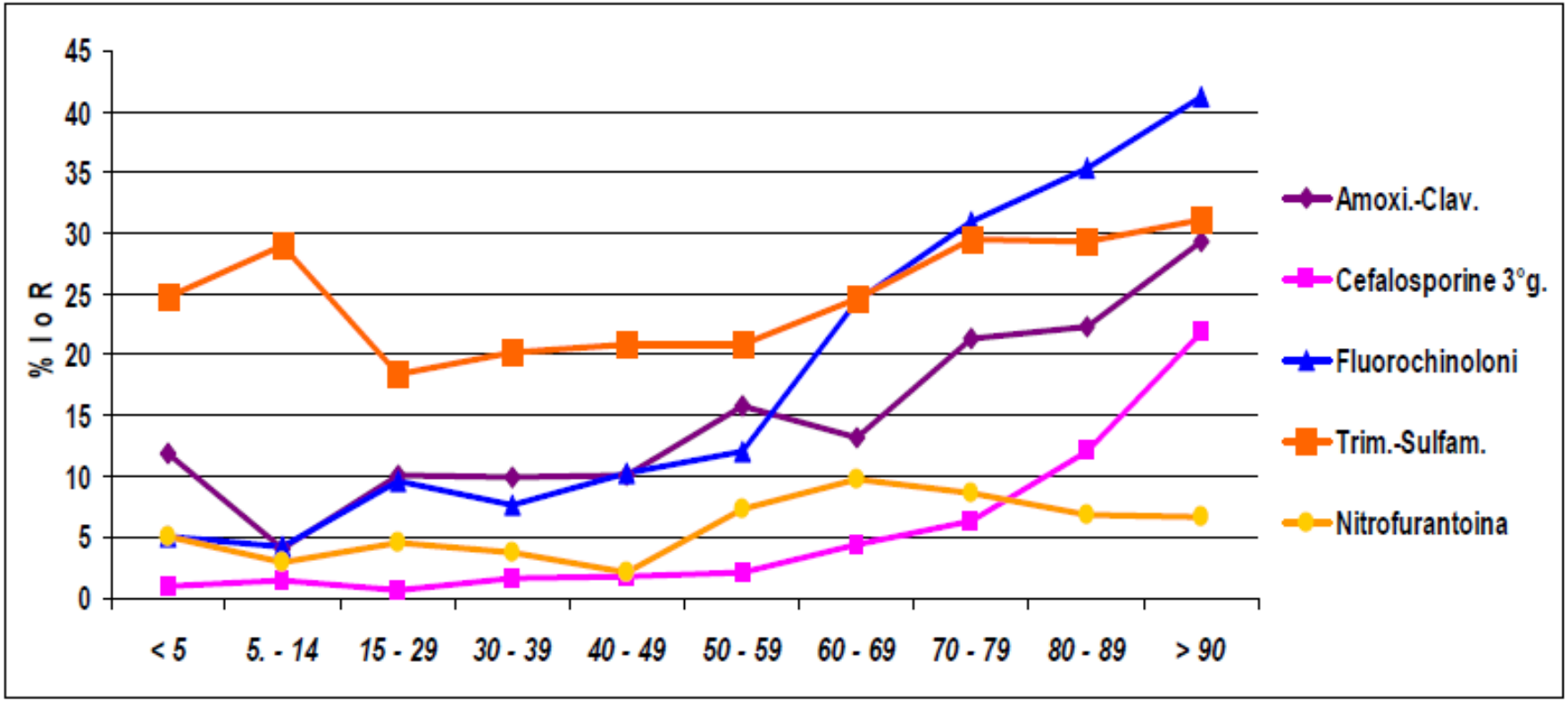
del Dipartimento di Patologia Clinica

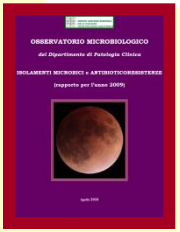
ISOLAMENTI MICROBICI e ANTIBIOTICORESISTENZE

(rapporto per l'anno 2009)

Aprile 2010

E. coli – urine – anno 2009





AREE TEMATICHE
- Diabete
- Privacy
- Screening
- Oncologia
- Farmaci
- Osservatorio Microbiologico
- Comitato Controllo Infezioni
  - Prevenzione
  - Sorveglianza
    - Comunicazione Eventi Epidemici
    - Sicher
    - Sitier
  - Lotta alla sepsi
  - Link

SORVEGLIANZA

La Sorveglianza costituisce il secondo fondamentale pilastro della Lotta alle Infezioni Correlate all'Assistenza Sanitaria.

ASSR ER Doss.123 "Epidemie di infezioni correlate all'assistenza sanitaria - Sorveglianza e controllo"

Sorveglianza attiva sugli Enterobatteri produttori di carbapenemasi

L'emergere della resistenza ai carbapenemi negli enterobatteri costituisce un problema clinico rilevante, dato che questi antibiotici rappresentano i farmaci di riferimento per la terapia delle infezioni invasive da enterobatteri Gram negativi multiresistenti. Tale resistenza è dovuta prevalentemente
all'emergere di nuove β-lattamasi capaci di idrolizzare i carbapenemi.
Gli Enterobatteri resistenti ai carbapenemi, non sono solo un problema rilevante sul piano clinico, ma rappresentano anche un pericolo notevole per la sanità pubblica per diversi motivi:
□ gli Enterobatteri sono molto frequentemente causa di infezioni, in ambito sia ospedaliero che
comunitario, e la progressiva diffusione di ceppi resistenti ai carbapenemi renderebbe problematico il trattamento di un

I microrganismi MDR

Viene definita "Multi Drug Resistance" una resistenza ad almeno tre classi diverse di antibiotici

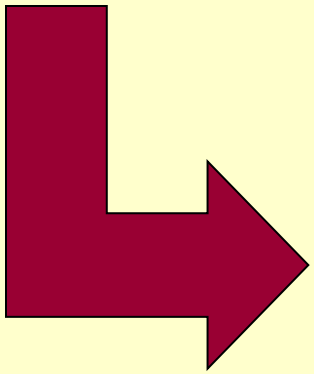
Es. : beta-lattamici + chinoloni + aminoglicosidi….

I microrganismi MDR

- S. aureus Meticillina R (MRSA)
- Enterococchi Vancomicina R (VRE)
- A. baumannii S solo a colistina
- P. aeruginosa S solo a colistina
- Enterobatteri S solo a colistina e/o carbapenemi (ESBL+ o AmpC+)

L'impatto clinico

1. Minore probablità di successo della terapia empirica
2. Notevoli problemi anche nella terapia mirata (maggiore tossicità e/o costo a volte senza corrispondente aumento di efficacia)

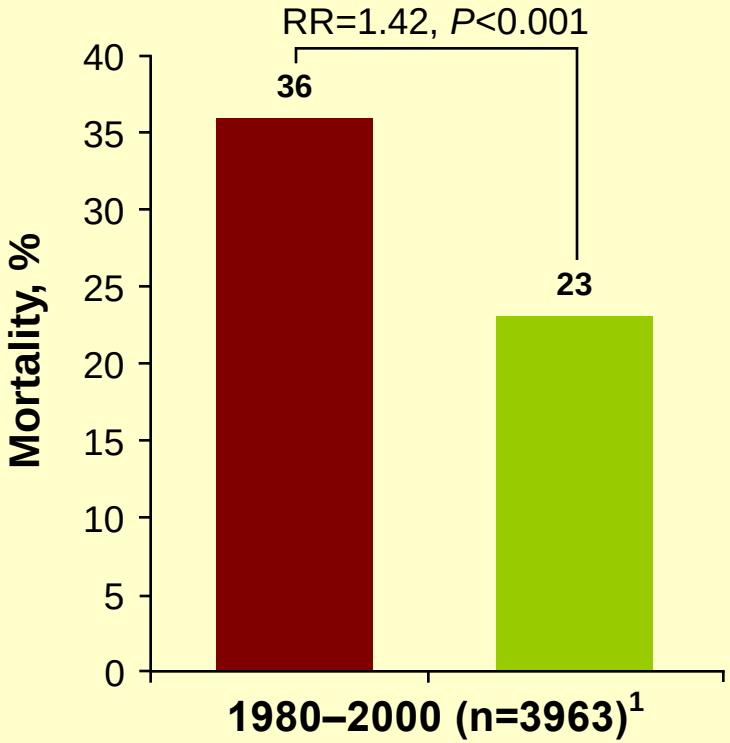


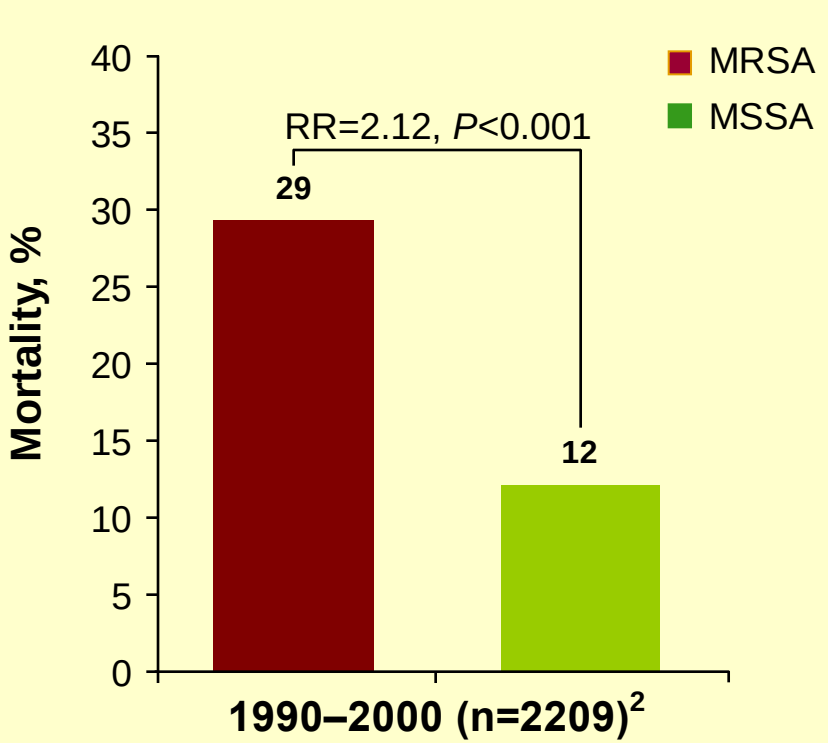
incremento

- costi
- complicanze
- tempi di degenza
- mortalità

Impact of methicillin-resistance on mortality in *S. aureus* bacteraemia

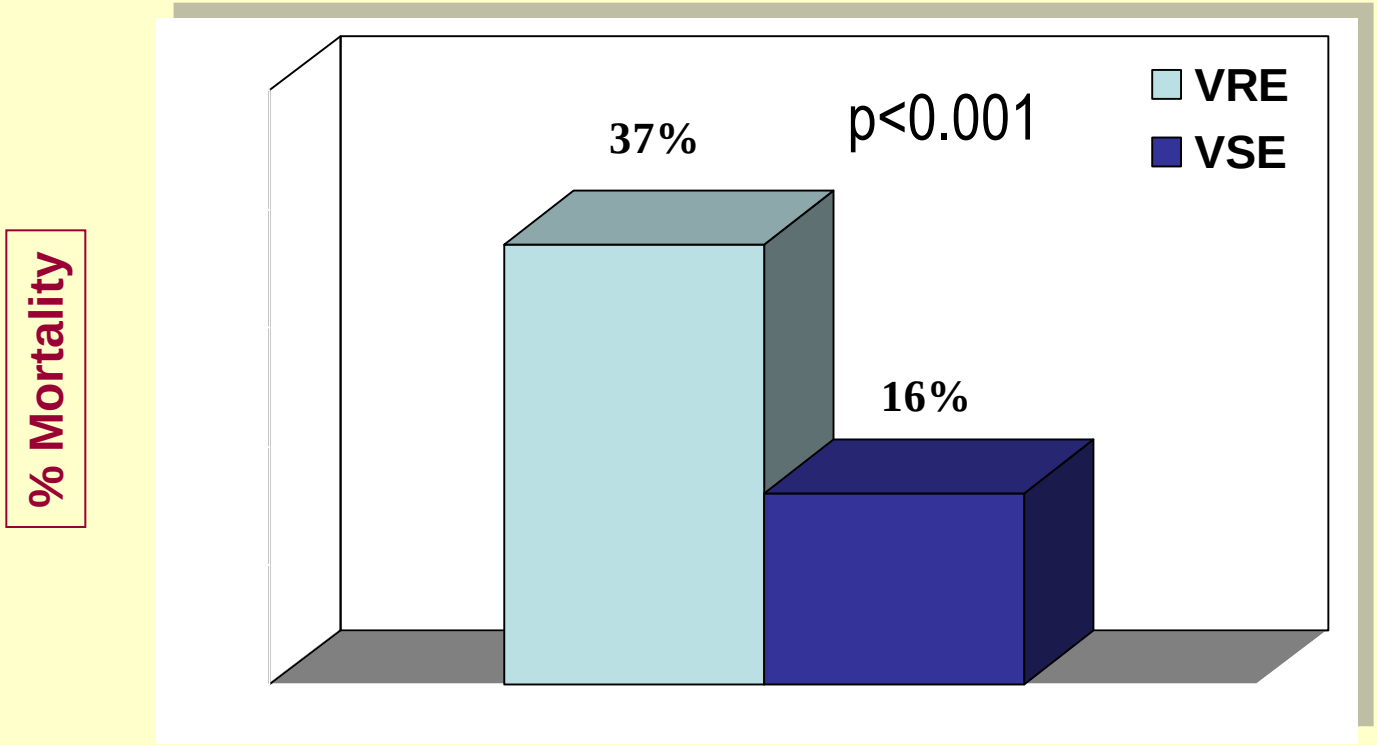
Mortality in *S. aureus* bacteraemia: the results of two meta-analyses





1. Cosgrove S *et al*. *Clin Infect Dis* 2003;36:53–59
2. Whitby M *et al*. *Med J Aust* 2001;175:264–267

Impatto della Vancomicina R nelle batteriemie da Enterococco



CDC. MMWR 1993;42:597-599

MINIREVIEW

Clinical and Economic Impact of Common Multidrug-Resistant Gram-Negative Bacilli[▽]

Christian G. Giske,[1]* Dominique L. Monnet,[2]† Otto Cars,[3] and Yehuda Carmeli[4,5] on behalf of ReAct-Action on Antibiotic Resistance

nelle infezioni invasive da :

Enterobatteri ESBL+

P. aeruginosa MDR

A. baumannii MDR

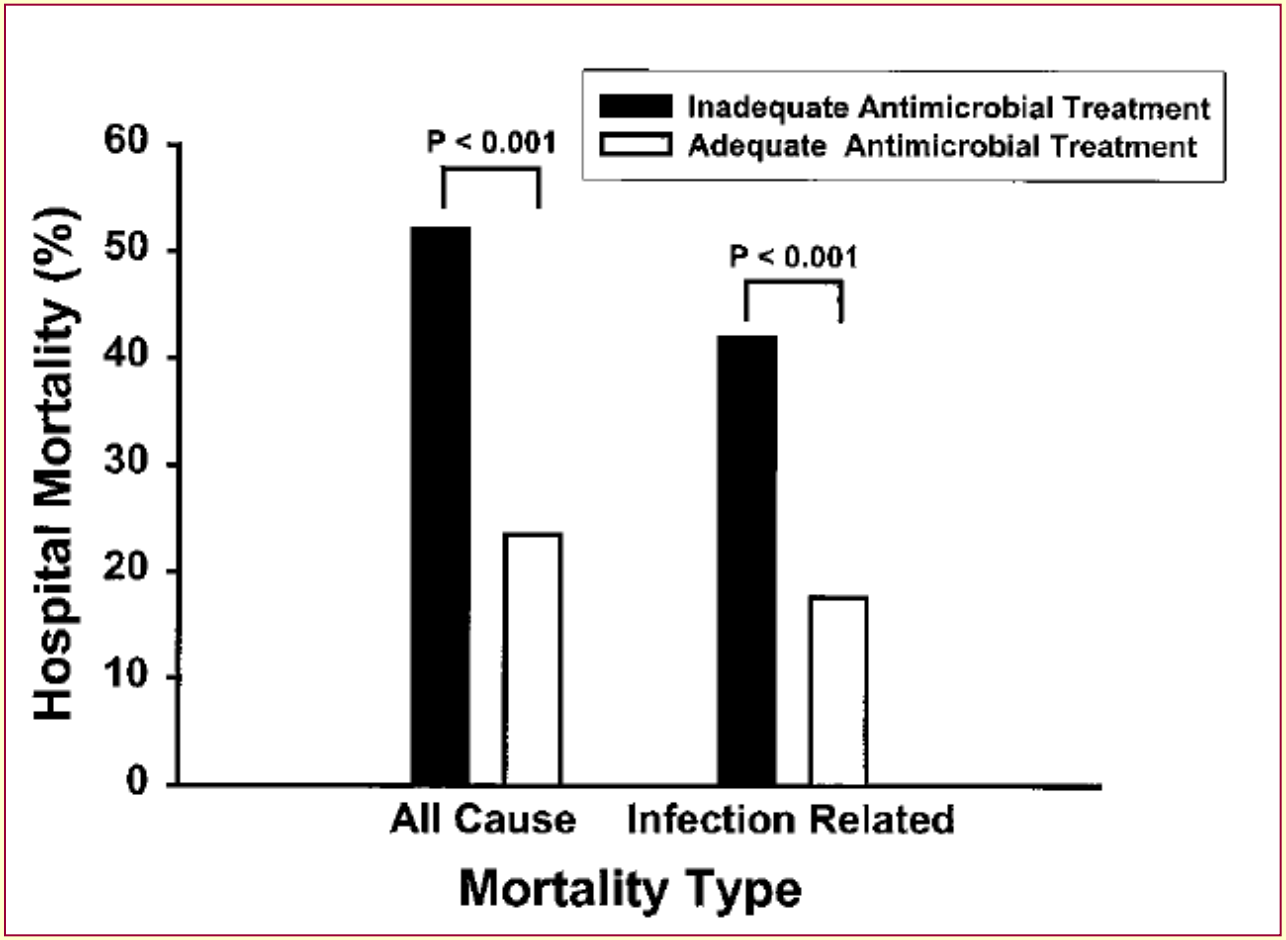
↑ degenza ↑ costi

↑ mortalità

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2008, p. 813–821

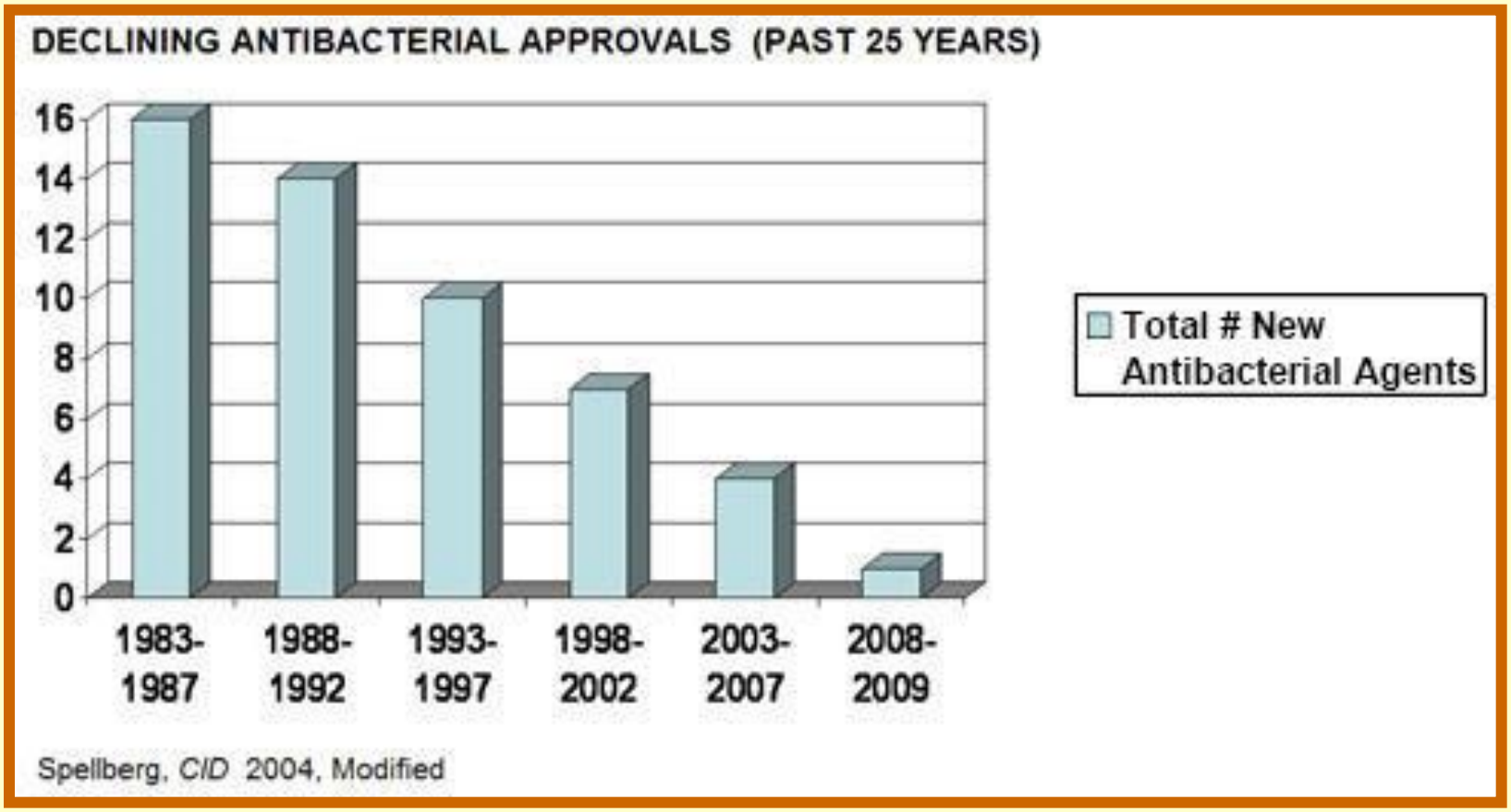
Inadequate Antimicrobial Treatment of Infections

Marin H. Kollef, MD, FCCP; Glenda Sherman, RN; Suzanne Ward, RN; and Victoria J. Fraser, MD

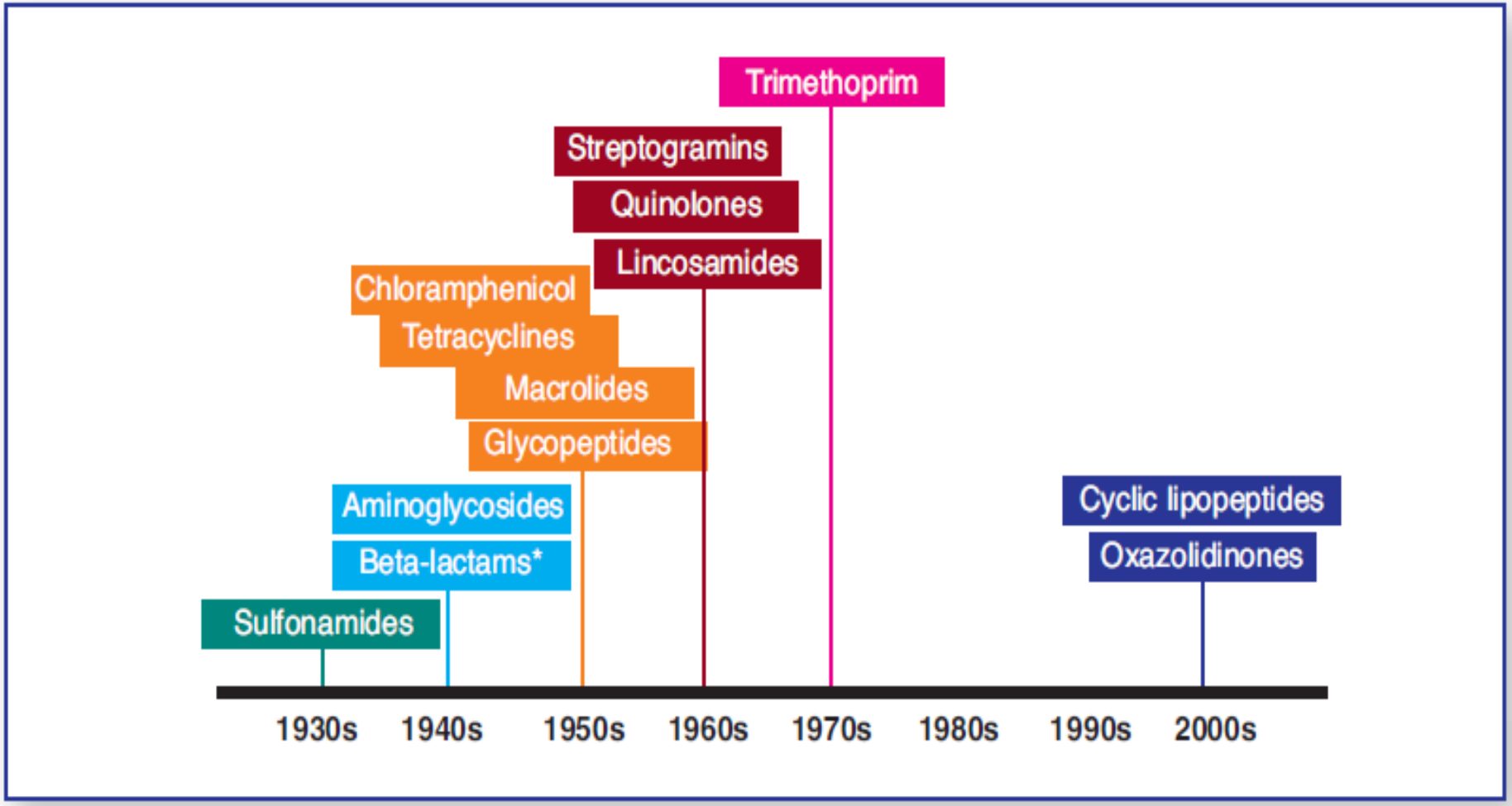


(CHEST 1999; 115:462–474)

La scarsità di nuovi antibiotici

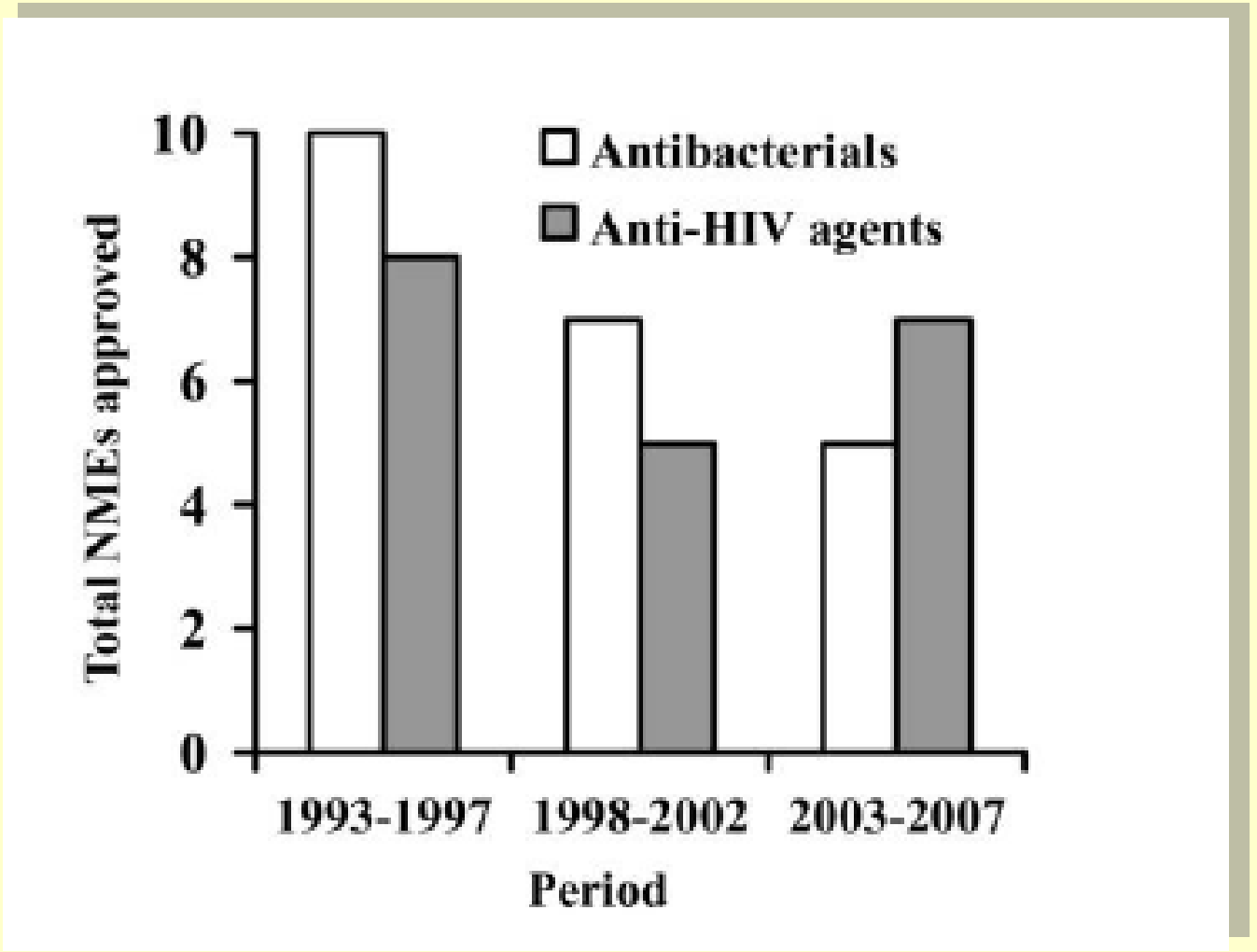


Nuove molecole antibatteriche approvate dalla FDA


Trimethoprim
Streptogramins
Quinolones
Lincosamides
Chloramphenicol
Tetracyclines
Macrolides
Glycopeptides
Aminoglycosides
Beta-lactams*
Sulfonamides
Cyclic lipopeptides
Oxazolidinones
1930s
1940s
1950s
1960s
1970s
1980s
1990s
2000s

Le ragioni del crollo della ricerca di nuovi antibatterici

- Le terapie antibiotiche sono sostanzialmente di breve durata (….molto meno "remunerative" di quelle per le patologie croniche)


Antibacterials
Anti-HIV agents
Total NMEs approved
10
8
6
4
2
0
1993-1997
1998-2002
2003-2007
Period

Le ragioni del crollo della ricerca di nuovi antibatterici

- Le terapie antibiotiche sono sostanzialmente di breve durata (….molto meno "remunerative" di quelle per le patologie croniche)
- Le molecole perdono di efficacia nel tempo per lo sviluppo delle resistenze
- Le politiche di corretta gestione del farmaco tendono a limitare l'utilizzo delle nuove molecole

Le campagne di sensibilizzazione

National Campaign for Appropriate Antibiotic Use in the Community

1995

Campaign to Prevent Antimicrobial Resistance

Centers for Disease Control and Prevention
National Center for Infectious Diseases
Division of Healthcare Quality Promotion

Clinicians hold the solution!

- *Link to: Campaign to Prevent Antimicrobial Resistance Online*
- *Link to: Federal Action Plan to Combat Antimicrobial Resistance*

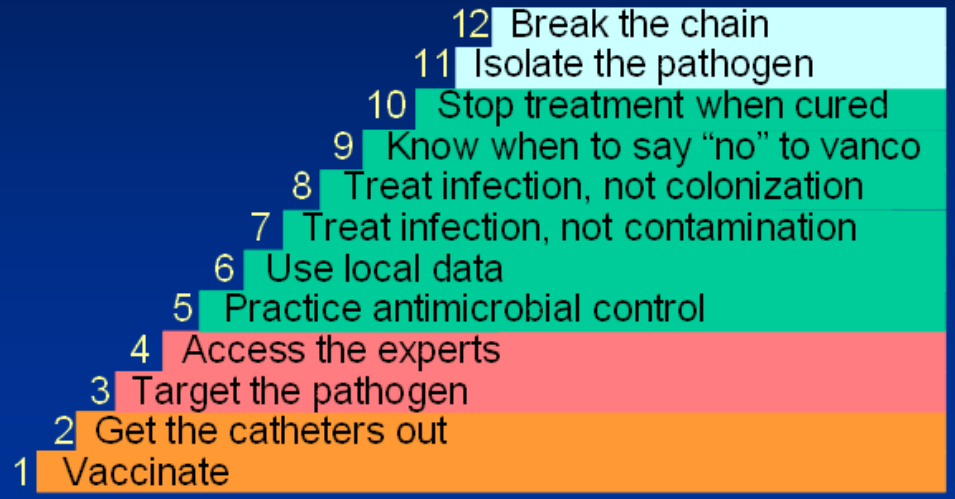
CDC
Centers for Disease Control and Prevention

Key Prevention Strategies

- Prevent infection
- Diagnose and treat infection effectively
- Use antimicrobials wisely
- Prevent transmission

CDC
Centers for Disease Control and Prevention

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults



CDC
Centers for Disease Control and Prevention

Use Antimicrobials Wisely

Step 10: Stop treatment when infection is cured or unlikely

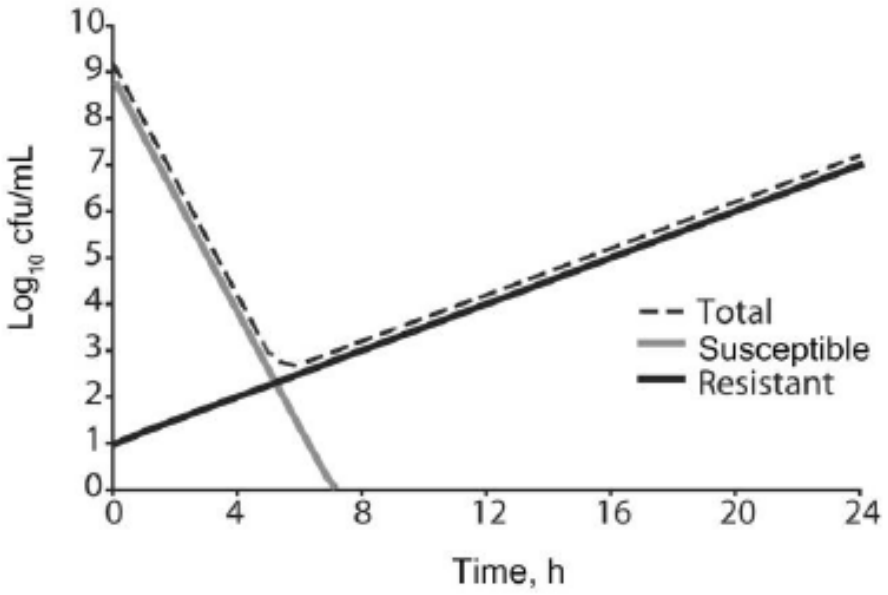
Fact: Failure to stop unnecessary antimicrobial treatment contributes to overuse and resistance.

CDC
Centers for Disease Control and Prevention

Optimizing Drug Exposure to Minimize Selection of Antibiotic Resistance

Sara K. Olofsson and Otto Cars

Antibiotic Research Unit, Department of Medical Sciences, Clinical Bacteriology and Infectious Diseases, Uppsala University, Uppsala, Sweden



Clinical Infectious Diseases 2007;45:S129–36

GET SMART...

- Antibiotics are strong medicines, but they don't cure everything.
- When not used correctly, antibiotics can actually be harmful to your child's health.
- Antibiotics can cure most bacterial infections. Antibiotics cannot cure viral illnesses.
- Antibiotics kill bacteria – not viruses.
- When your child is sick, antibiotics are not always the answer.

USE ANTIBIOTICS WISELY

Talk with your healthcare provider about the right medicines for your child's health.

For more information, see the Centers for Disease Control and Prevention website at:
www.cdc.gov/getsmart or call 1-800-CDC-INFO

FOR PARENTS

GET SMART

Know When Antibiotics Work

Snort. Sniffle.
Sneeze.
No Antibiotics
Please.

GET SMART…

- Antibiotics are strong medicines, but they don't cure everything.
- When not used correctly, antibiotics can actually be harmful to your health.
- Antibiotics can cure most bacterial infections. Antibiotics cannot cure viral illnesses.
- Antibiotics kill bacteria – not viruses.
- When you are sick, antibiotics are not always the answer.

USE ANTIBIOTICS WISELY

Talk with your healthcare provider about the right medicines for your health.

GET SMART

Know When Antibiotics Work

Cold or Flu.
Antibiotics Don't
Work for You.

For more information, see the Centers for Disease Control and Prevention website at:
www.cdc.gov/getsmart or call 1-800-CDC-INFO

GET SMART

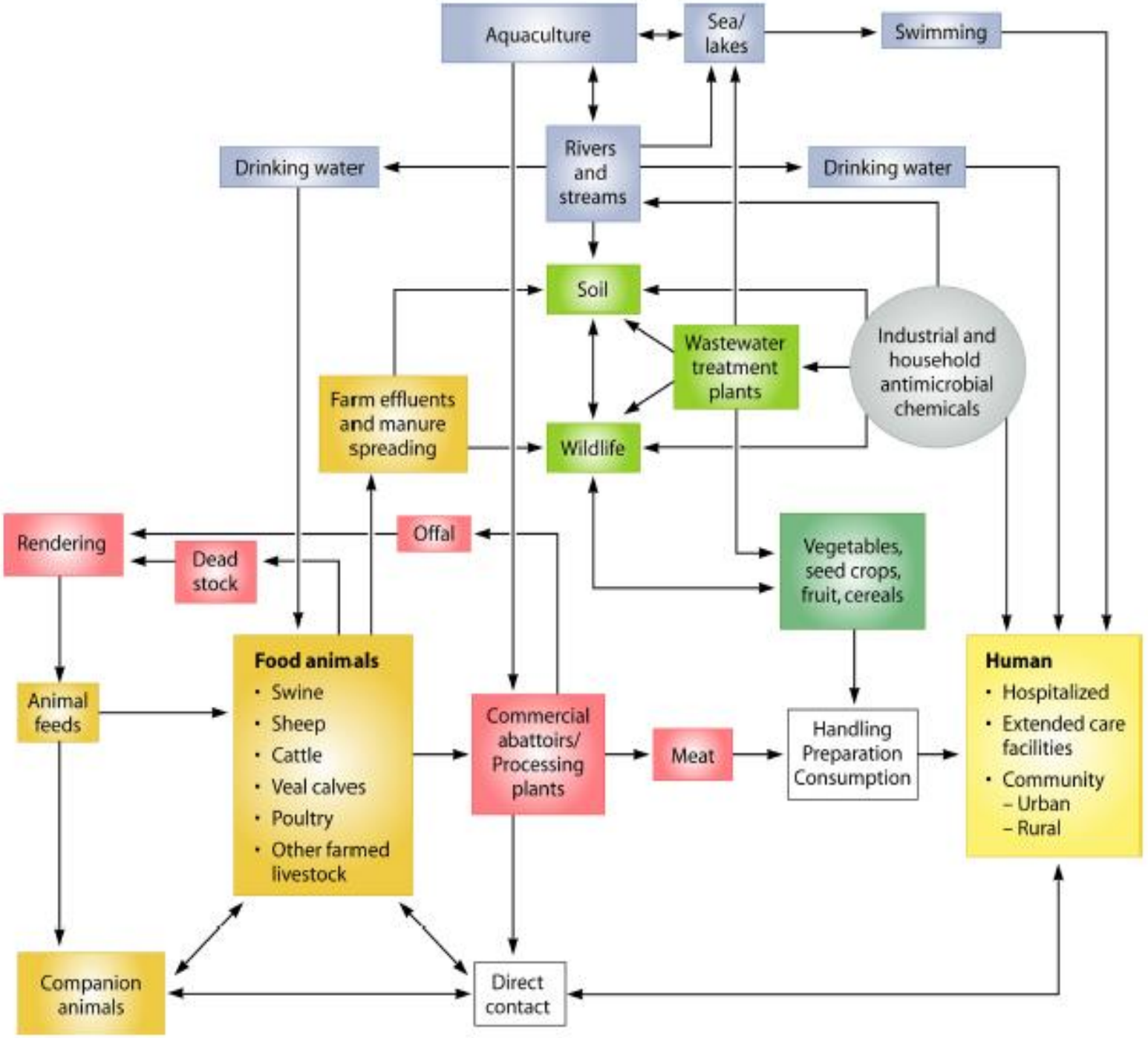
Know When Antibiotics Work On The Farm

Enteric Diseases Epidemiology Branch

Division of Foodborne, Bacterial and Mycotic Diseases

National Center for Zoonotic, Vectorborne, and Enteric Diseases

Centers for Disease Control and Prevention


Aquaculture
Sea/ lakes
Swimming
Rivers and streams
Drinking water
Drinking water
Soil
Wastewater treatment plants
Industrial and household antimicrobial chemicals
Farm effluents and manure spreading
Wildlife
Rendering
Dead stock
Offal
Vegetables, seed crops, fruit, cereals
Animal feeds
Food animals
• Swine
• Sheep
• Cattle
• Veal calves
• Poultry
• Other farmed livestock
Commercial abattoirs/ Processing plants
Meat
Handling Preparation Consumption
Human
• Hospitalized
• Extended care facilities
• Community
– Urban
– Rural
Companion animals
Direct contact

WHO Global Strategy for Containment of Antimicrobial Resistance

2001

CHAPTER 4

Use of antimicrobials in food-producing animals

2001

Bad Bugs, No Drugs

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews

IDSA
Infectious Diseases Society of America

July 2004

Lives Devastated by Antibacterial Resistant Organisms

IDSA

Carlos Don's Story
A healthy 12-year old athlete from Southern California who died of pneumonia caused by an MRSA infection

Posted: Jun

Posted: June 2007

Bryce's Story: A Family Hopes
A healthy 14-month old from Santee, California who contracted MRSA and spent many harrowing weeks in the intensive care unit as doctors struggled to save his life

Posted: May 2007

Ricky Lannetti's Story
A healthy 21-year old football player at Lycoming College in Williamsport, Pennsylvania who contracted MRSA and did not survive the infection

Posted: April 2007

Dee Dee Wallace's Story
A Wisconson woman nearly loses her leg, and her life, to MRSA

Posted: September 2007

Brandon Noble's Story
Washington Redskins defensive tackle who has had recurring serious MRSA infections in his knee
Posted: March 2006

Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John E. Edwards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]

The "Strategies To Address Antimicrobial Resistance (STAAR)" Act

Clinical Infectious Diseases 2009; 48:1–12

I metodi per controllare l'uso inappropriato degli antibiotici quali :

- la disincentivazione alla pratica comune di utilizzarli nelle patologie virali

- la regolamentazione dell'utilizzo in agricoltura

- il divieto di utilizzarli come promotori della crescita negli allevamenti….

… non sono la soluzione del problema ma possono darci tempo per trovare la vera soluzione del problema

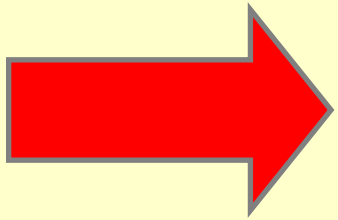
IDSA

The 10 × '20 Initiative: Pursuing a Global Commitment to Develop 10 New Antibacterial Drugs by 2020

Infectious Diseases Society of America[a]
Infectious Diseases Society of America, Arlington, Virginia

Clinical Infectious Diseases 2010;50:1081–1083

The time has come for a global commitment to develop new antibacterial drugs. Current data document the impending disaster due to the confluence of decreasing investment in antibacterial drug research and development concomitant with the documented rapid increase in the level of resistance to currently licensed drugs. Despite the good faith efforts of many individuals, professional societies, and governmental agencies, the looming crisis has only worsened over the past decade.



Bad Bugs Need Drugs

10x'20

Ten new **ANTIBIOTICS** by 2020

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

emea
European Medicines Agency

TECHNICAL REPORT

The bacterial challenge: time to react

A call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents

2009

The evolving threat of antimicrobial resistance

Options for action

World Health Organization

2012

18 NOVEMBRE 2012

Giornata Europea degli Antibiotici

Un'iniziativa europea per la salute

European Centre for Disease Prevention and Control

COLD? FLU? TAKE CARE NOT ANTIBIOTICS

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

SURVEILLANCE REPORT

Antimicrobial resistance surveillance in Europe

2011

Figure 4.38: *Staphylococcus aureus*: percentage (%) of invasive isolates resistant to meticillin (MRSA), by country, EU/EEA countries, 2008–2011

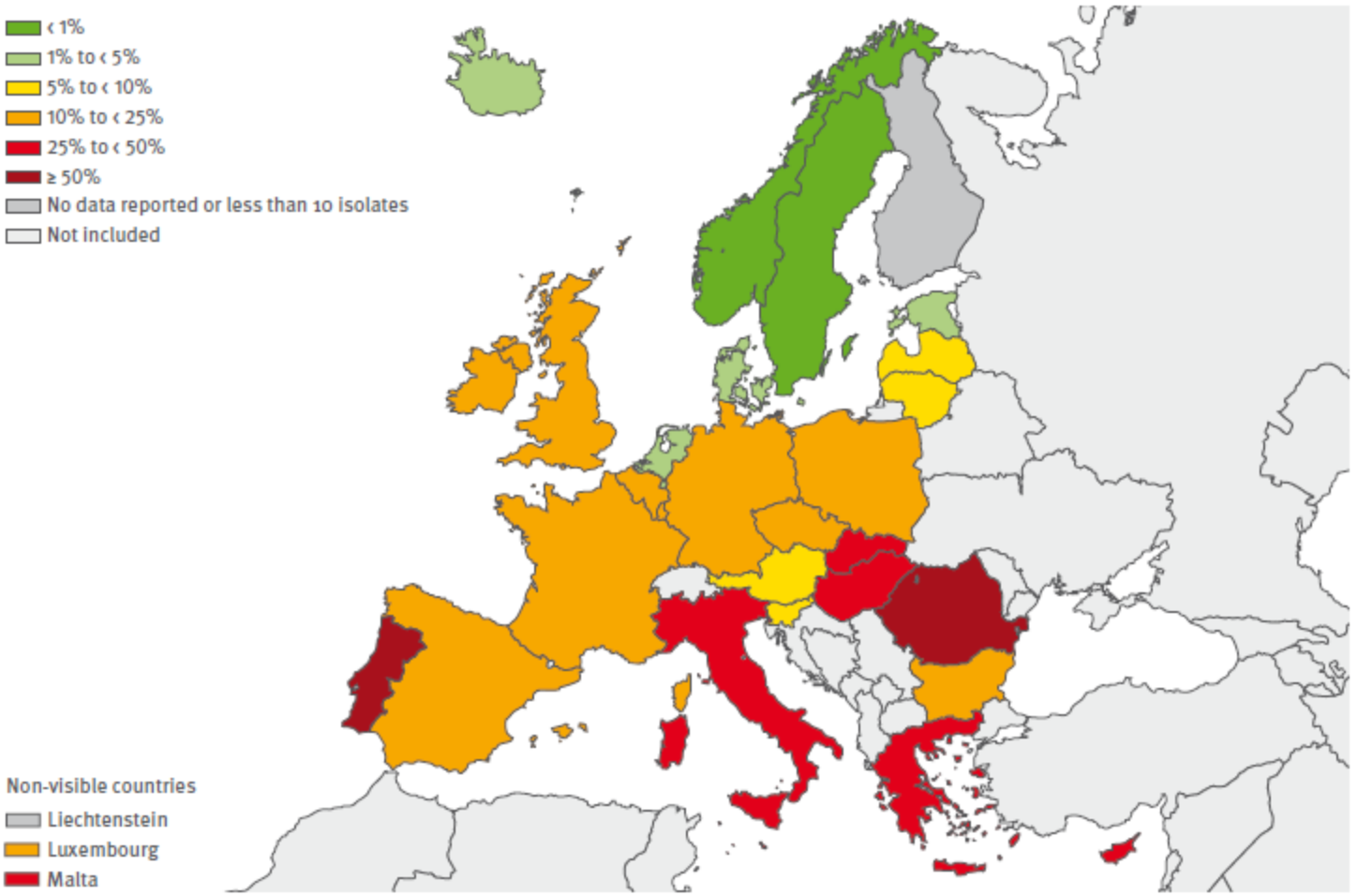


Figure 4.1: *Escherichia coli*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by country, EU/EEA countries, 2011

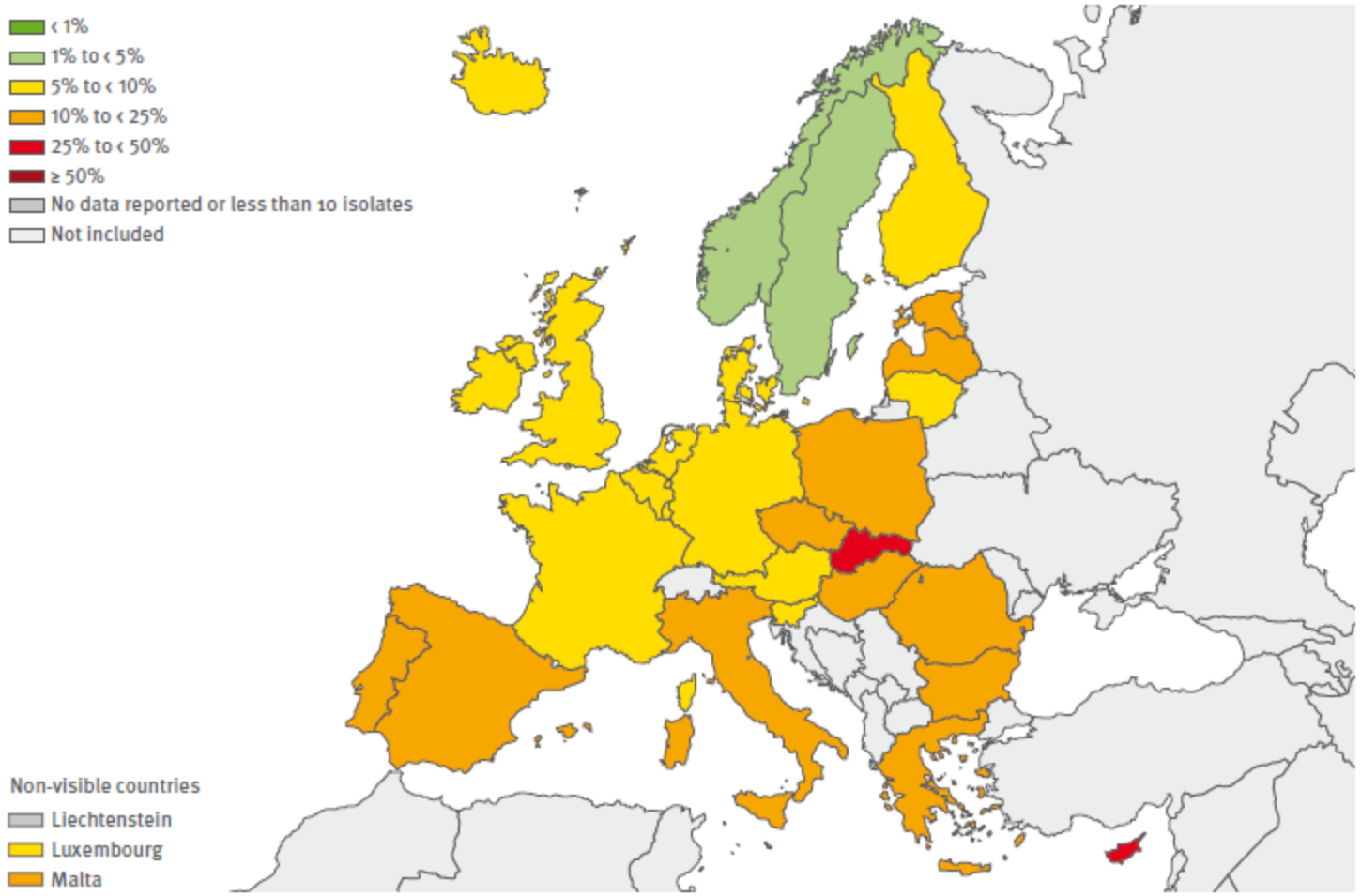


Figure 4.2: *Escherichia coli*: percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2011

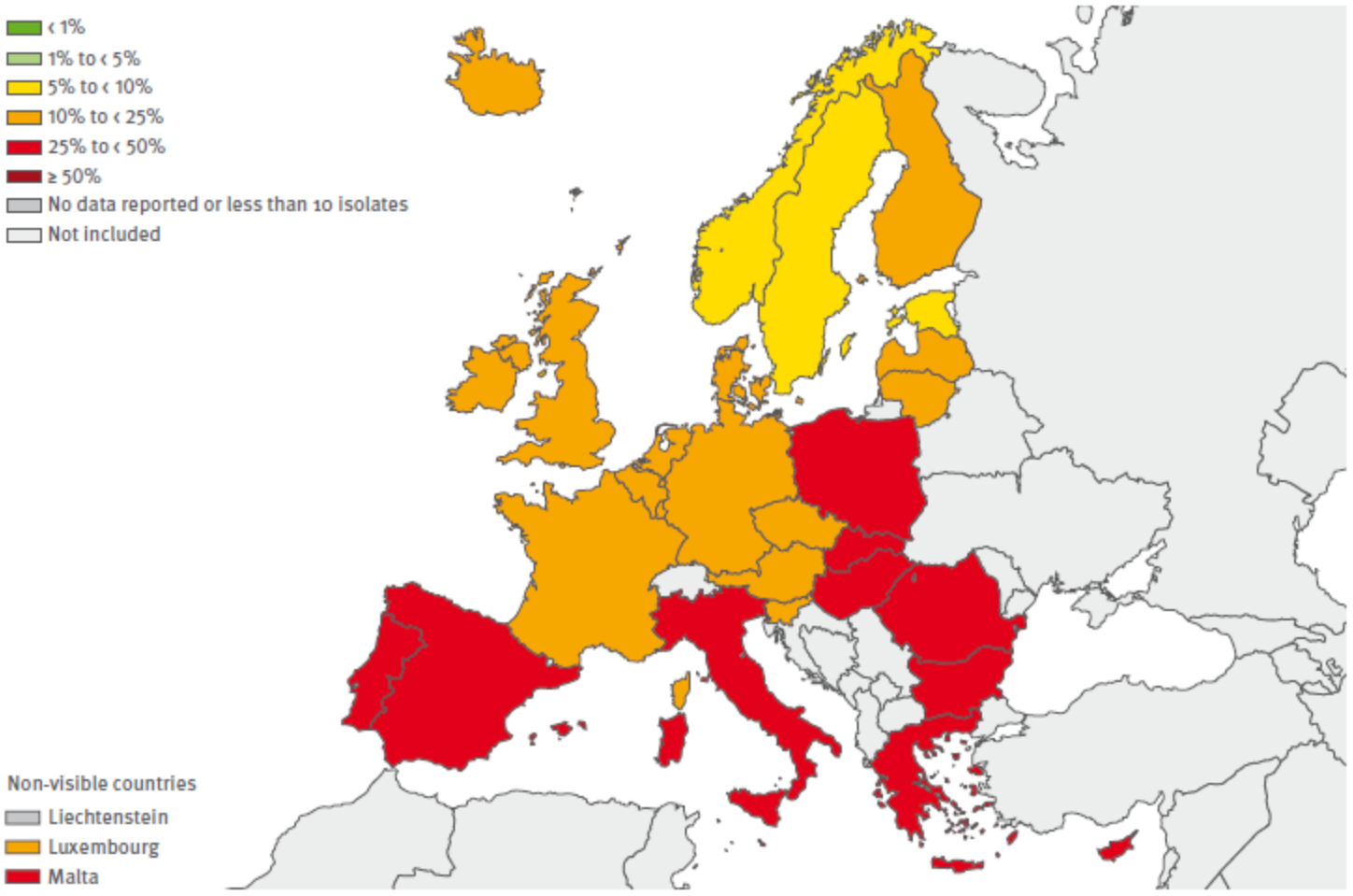


Figure 4.9: *Klebsiella pneumoniae*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2011

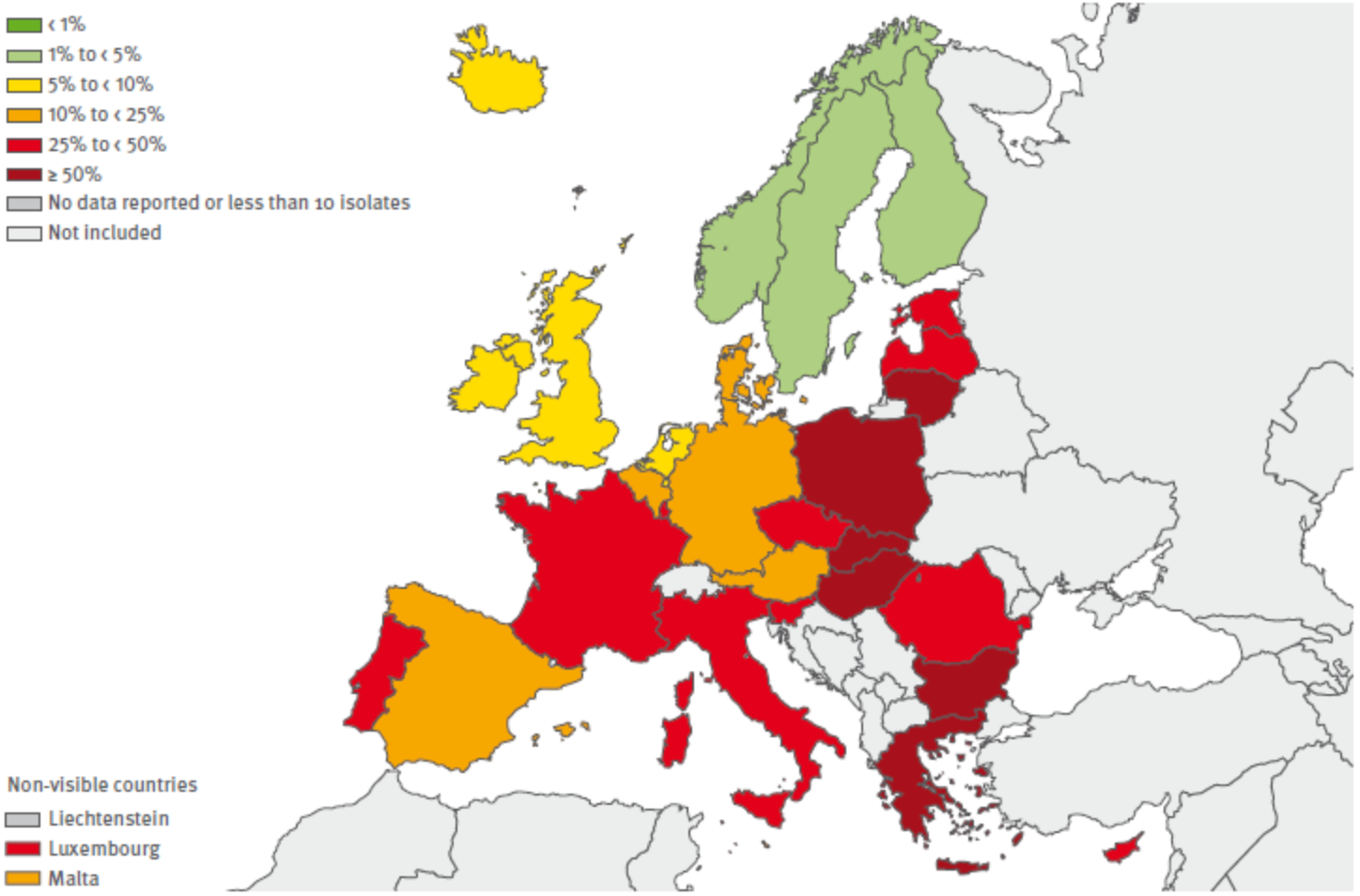


Figure 4.10: ***Klebsiella pneumoniae*: percentage (%) of invasive isolates with resistance to fluoroquinolones, by country, EU/EEA countries, 2011**

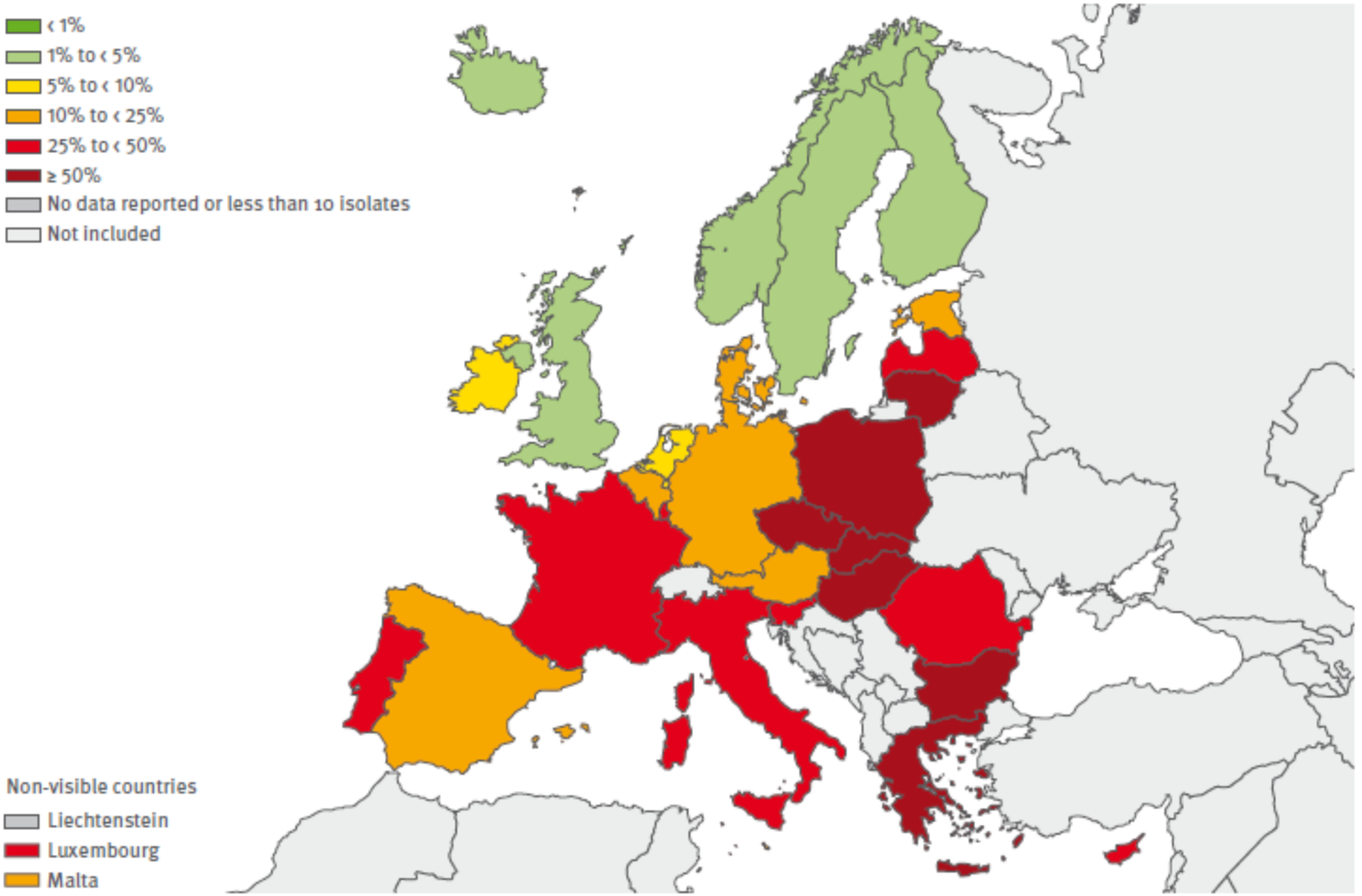
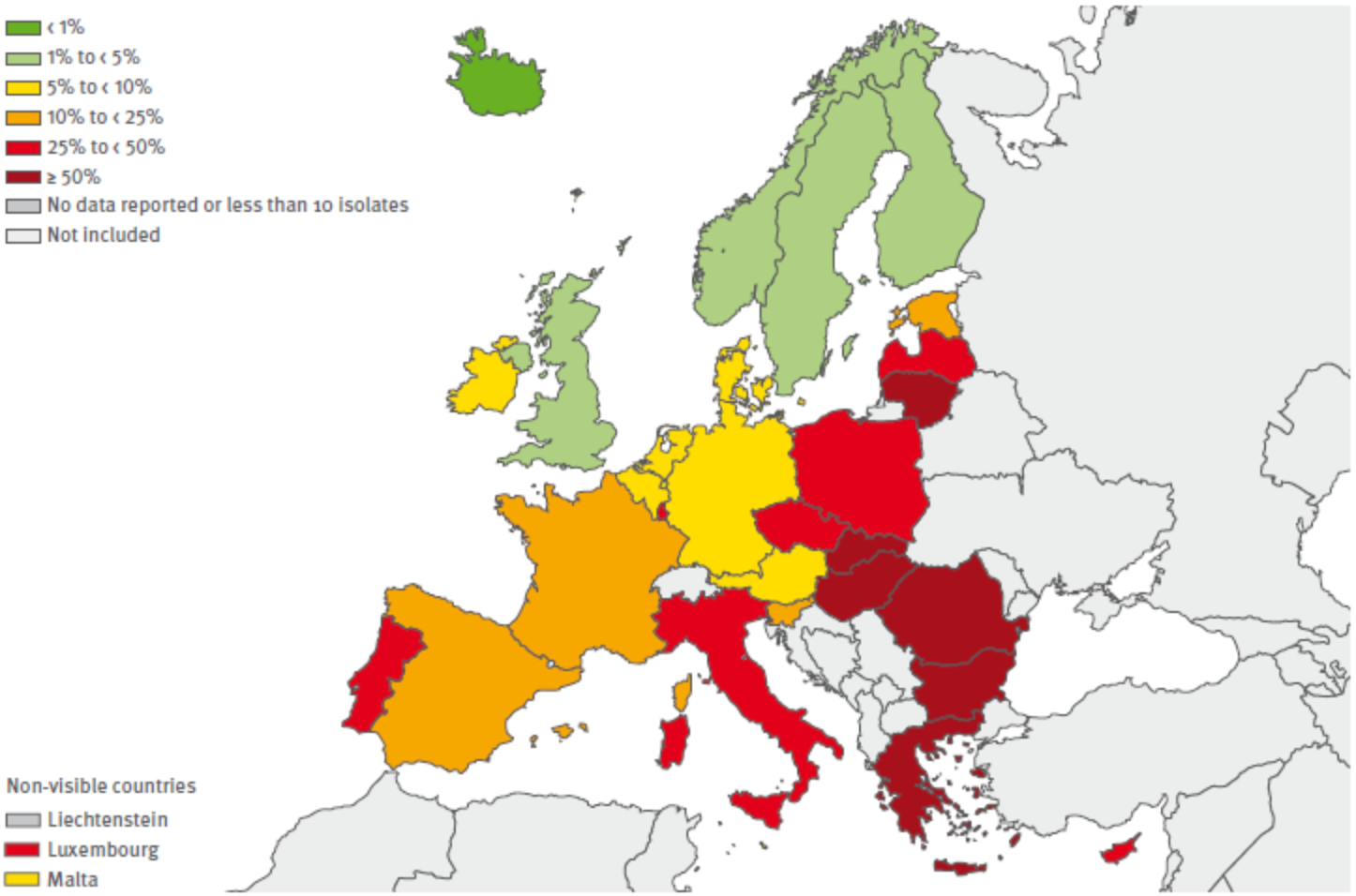
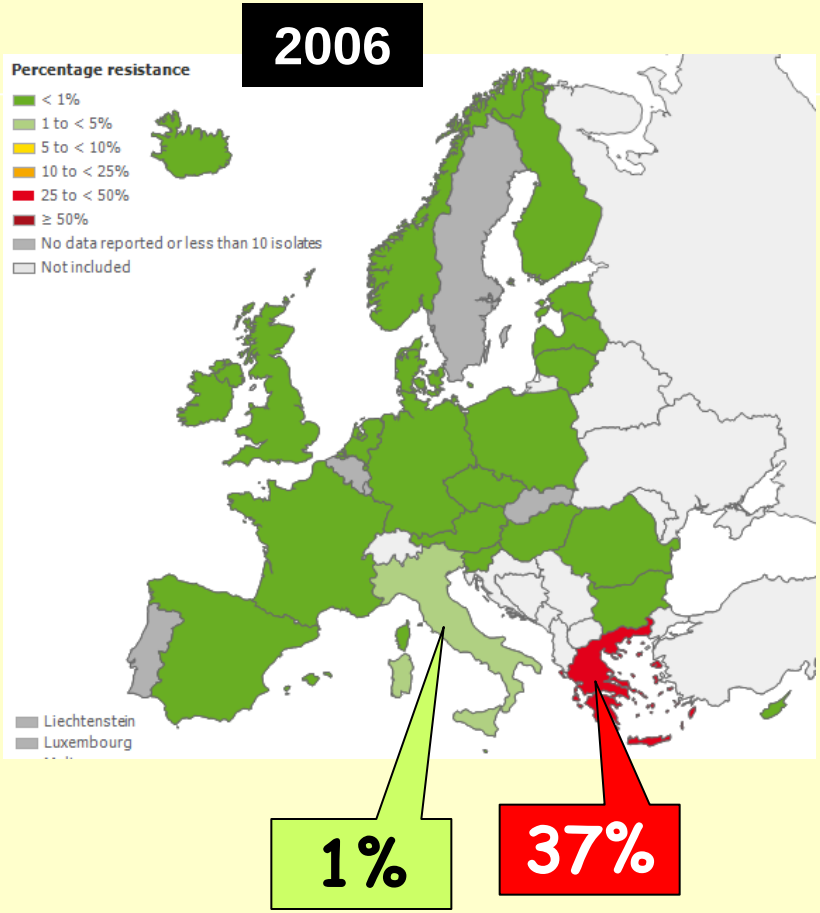
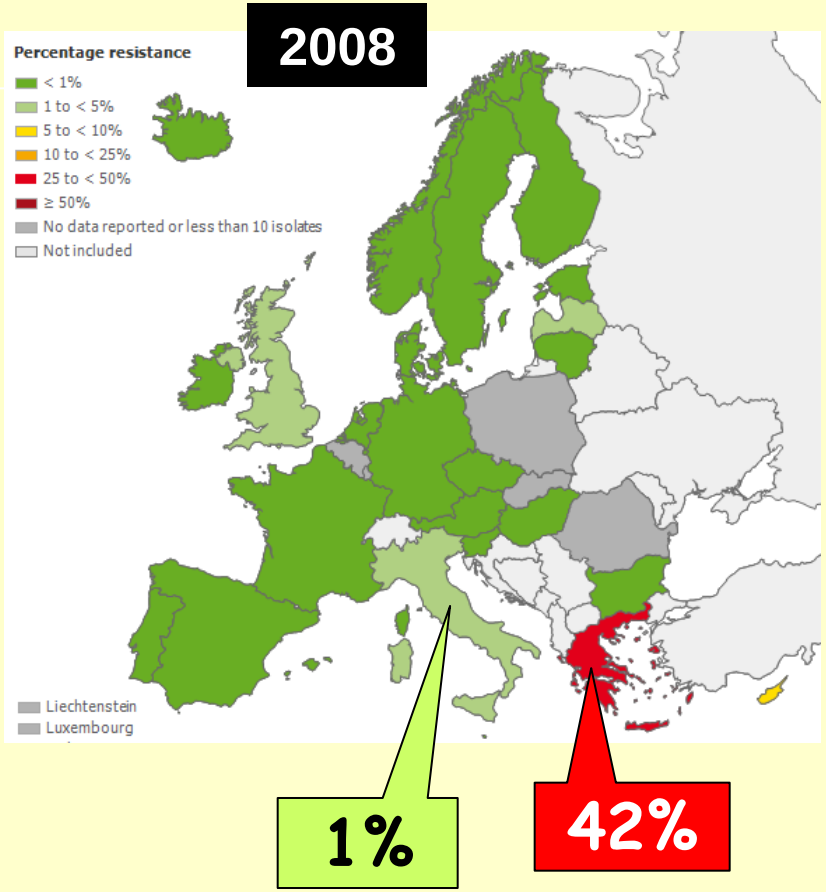


Figure 4.11: ***Klebsiella pneumoniae*****: percentage (%) of invasive isolates with resistance to aminoglycosides, by country, EU/EEA countries, 2011**



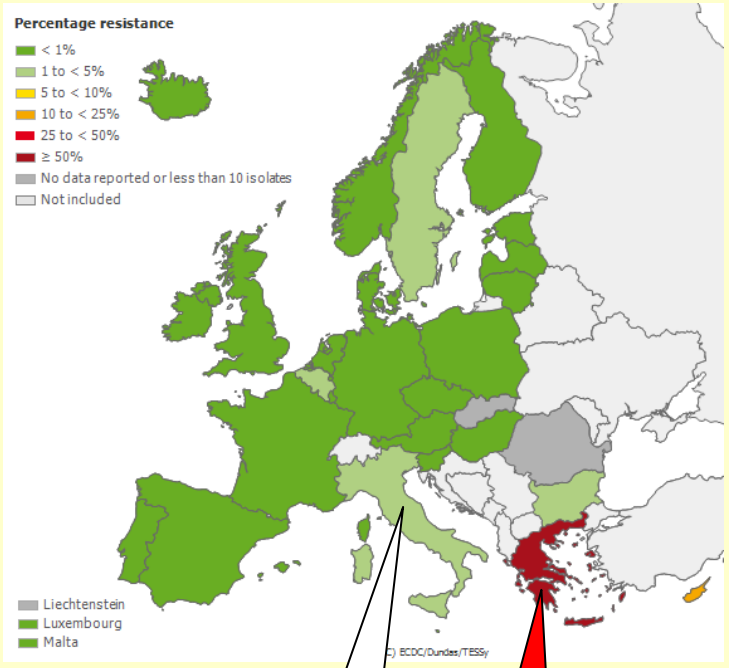
K. pneumoniae R ai carbapenemi



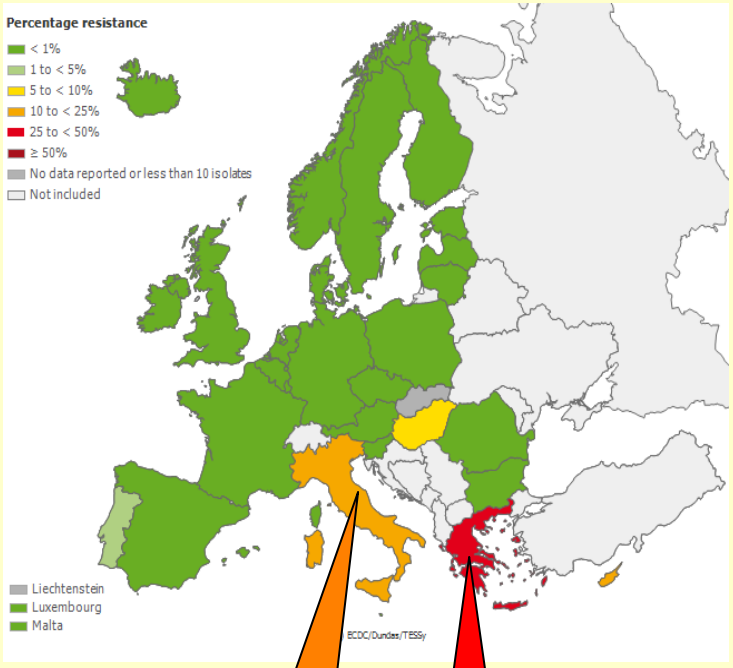


K. pneumoniae R ai carbapenemi

2009



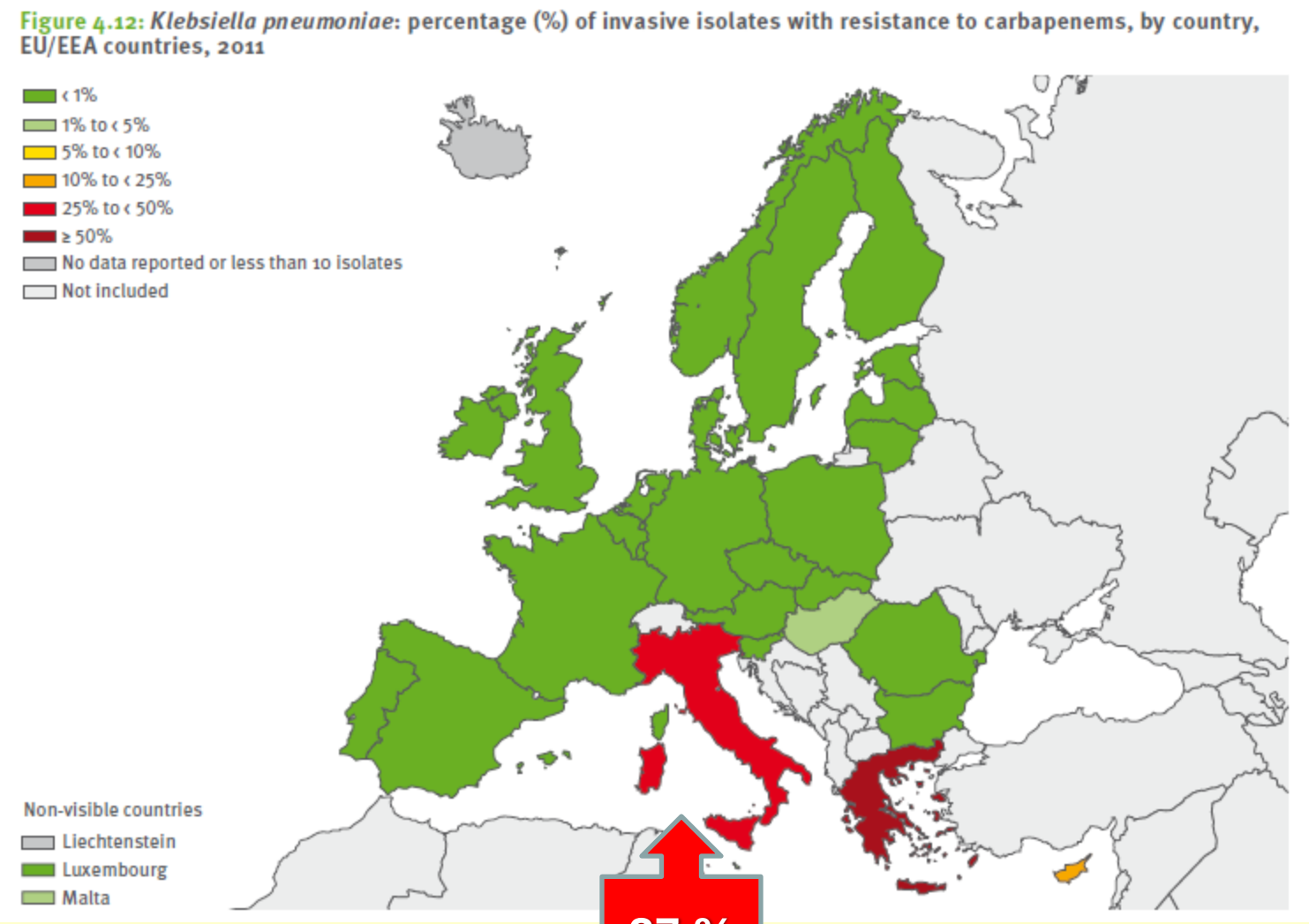
2010



EARSS database

K. pneumoniae R ai carbapenemi

2011



I super batteri minacciano l'Europa - Corriere della Sera - Microsoft Internet Explorer provided by Az

http://www.corriere.it/salute/11_novembre_18/superbatteri-minacciano-europa_9617f8e2-11fa-11e1-8aad-a8

File Modifica Visualizza Preferiti Strumenti ?

Preferiti Siti suggeriti Customize Links Free Hotmail Raccolta Web Slice

I super batteri minacciano l'Europa - Corriere della Sera

IL RAPPORTO

I super batteri minacciano l'Europa

Aumenta, soprattutto in Italia, il tasso di infezioni resistenti agli antibiotici, soprattutto a causa dell'abuso che si fa di questi medicinali

Ceppi di E.coli

BRUXELLES - Ci si preoccupa tanto dei virus esotici che si affacciano di tanto in tanto all'orizzonte e di quelli influenzali che potrebbero dare origine a pandemie ben più gravi di quella da H1N1, ma in Europa ci sono già infezioni che fanno 25.000 morti l'anno e contro cui perfino la medicina moderna, con tutta la sua tecnologia e il suo armamentario farmacologico, si scopre impotente: sono le malattie da microrganismi resistenti agli antibiotici, una minaccia che non riguarda più solo i malati ricoverati in ospedale.

I DATI- I dati presentati ieri a Bruxelles, in occasione della Giornata di sensibilizzazione al corretto uso degli antibiotici, da Marc Sprenger, direttore del Centro europeo di controllo delle

NOTIZIE CORRELATE

- Malattie infettive: l'esperto risponde

OGGI IN salute ›

«Non dimentichiamo l'amianto»

Corriere della Sera

18 -11-2011

K. pneumoniae KPC +

Antibiotico	MIC mg/L(S/I/R)
Amp/Sulb	> 64 R
Pip/Tazo	>128 R
Ceftriaxone	>64 R
Ceftazidime	>64 R
Cefepime	>64 R
Ertapenem	>32 R
Imipenem	>8 R
Meropenem	>8R
Aztreonam	>64 R
Amikacina	>64 R
Gentamicina	>64 R
Tobramycina	>16 R
Ciprofloxacina	>4 R
Levofloxacina	>8 R
Colistina	0.5 S

Antibioticoresistenza :
un problema di tutti
che richiede l'impegno di tutti